JOURNAL OF

GENERAL CHEMISTRY

OF THE USSR

(ZHURNAL OBSHCHEI KHIMII)

IN ENGLISH TRANSLATION

$$\left(\frac{c}{b}\right)$$

SYNTHESES OF HETEROCYCLIC COMPOUNDS

Volumes 1 and 2 Edited by
A. L. MNDZHOIAN
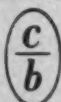
TRANSLATED FROM RUSSIAN

THE lack of a practical guide to the laboratory preparation of heterocyclic compounds is being met by this series of collections of synthesis methods, originally published by the Armenian Academy of Sciences.

The translation of Volumes 1 and 2 of this series is combined in this convenient handbook, devoted exclusively to the synthesis of furan derivatives.

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JOURNAL OF GENERAL CHEMISTRY OF THE USSR

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NEW TASKS OF CHEMICAL SCIENCE AND INDUSTRY

Outstanding achievements in industry, in agriculture, in the development of science and culture, and in the improvement of the material welfare of the working man greet our nation at the forthcoming 21st Convention of the Communist Party of the Soviet Union.

The Soviet nation under the guidance of the Communist Party has accomplished great transformations, making it possible for our country to enter a new and most important period of its development - a period of the expanded building of a communistic society. The main tasks of this period will be: the creation of a communism based on improved material technology, further strengthening of the economic might of our Country, and simultaneous with this a constantly more complete satisfaction of the growing material and spiritual needs of the Soviet people.

In the development of the national economy of the USSR for the next 15 years it is predicted that the decisive branches of USSR industry will increase their production by more than 2-3 times during this period. The prospective plan for the development of the national economy in the next 15 years is an economic program of the building of communism in the USSR, and the control figures for the development of the national economy during 1959-1965 are an integral part of this prospective plan. The main problem of the forthcoming seven years is an accelerated development of the national economy on the road to communism. The total industry production in 1965 when compared with 1958 will increase by approximately 80%, this being composed of an 85-88% increase in the production of Group "A", the manufacture of industrial machinery, and a 62-65% increase in the production of Group "B", the manufacture of consumer goods. The average annual increase in production during 1959-1965 for industry as a whole will be approximately 8.6%. If in 1952 a 1% increase in the total production (not including small secondary industry) represented 5 billion rubles, then in 1965 a similar increase will correspond to approximately 19 billion rubles, and the average annual increase in industrial production in the forthcoming seven-year plan will be nearly 135 billion rubles.

Special attention will be given to chemical developments. The chemical industry in the USSR was created during the Soviet regime. About 70 chemical plants were built even in the early five-year plans, including such giants as the mining and chemical combine "Apatite", the Bereznikov, Gorlov, Stalinogorsk, Voskresenskii, Nevsk and Konstantinova nitrate and superphosphate plants, the Solikamsk potash and Yaroslavl rubber-asbestos combines, and many others. The production of synthetic rubber by the S. V. Lebedev method began in our country many years before it did in either Germany or the United States, both having a highly developed chemical industry. The development of the chemical industry in our country also continued in subsequent years. In 1957 the total volume of chemical production in our country increased 112 times when compared with 1913, and 5 times when compared with 1940. At the present time the Soviet Union occupies second place in the world in the volume of chemical production.

The May Plenum of the Central Committee of the Communist Party of the Soviet Union promulgated the task of an accelerated development of the chemical industry, especially in the manufacture of synthetic materials, needed to satisfy the requirements of the population on the need for clothing, footwear, fabrics and articles of domestic and farm use, and also for the needs of industry, agriculture and construction. In the current report of Comrade N. S. Khrushchev entitled "Control Figures for the Development of the National Economy in the USSR During 1959-1965" it is proposed to increase the total volume of chemical production nearly 3 times in the next seven years. The production of synthetic materials should receive broad development: the output of chemical fibers to increase by 3.8-4 times, with that of the most valuable synthetic fibers to increase by 12-14 times, and the output of plastics and synthetic resins to increase 6.7 times. The production of mineral fertilizer

will be increased nearly 3 times, and there will be an especially large increase in the production of concentrated mineral fertilizers, more effective organophosphorus compounds for fighting plant pests and diseases, and also chemical weed-control agents.

The creation of a large-capacity synthetic materials industry is based on a utilization of naturally occurring gases and the by-product gases from the petroleum industry. The utilization of the by-product gases from the petroleum industry in the production of synthetic rubber will make it possible to effect a saving of about 1.3 billion rubles in capital expenditure in the next seven years. The production of nitrogen-containing fertilizers will also be based mainly on the utilization of naturally occurring gases, which will permit setting free about 4 billion rubles of capital outlay.

The large-scale production of new types of synthetic materials will make it possible to sharply expand the output of high-quality and cheap articles of common use. In the next seven years it will be necessary to build and complete the construction of more than 140 large chemical plants and to rebuild more than 130 plants. The creation of large combination plants for the complex processing of by-product gases from the petroleum industry, naturally occurring gases, gases from petroleum-refining plants, and other types of raw material, is planned.

Soviet science comes to the 21st Convention of the Communist Party of the Soviet Union with magnificent conquests, sounding out to the whole world. The majestic program of an expanded communistic development in our country, outlined in the report of Comrade N. S. Khrushchev, inspires Soviet scientists to the winning of new heights in world science.

At the present time our country has available a vast base of science material and an army of thousands of scientists. Besides the Academy of Sciences, only the laboratories of 9 universities and of several other higher schools occupied themselves with science in czarist Russia, and at the present time there are about 1000 institution of higher learning in the USSR, including such as the gigantic Moscow State University, several thousand research departments of various institutes in the fields of industry, agriculture, public health, etc., the center of science — The Academy of Sciences of the USSR with its institutes and laboratories, as well as the scientific academies of the different Soviet Rupublics. All of this creates a great potential for solving the principal and most important problems in science.

Although it was stated as early as last May in the report delivered by Comrade N. S. Krushchev to the Plenum of the Communist Party of the Soviet Union that Soviet scientists have made notable contributions in the field of chemical science, there still exists a noticeable lag in some of its ramifications. This primarily refers to the field of synthetic fibers and plastics. Insufficient attention is still being given to the research problems connected with the production and use of synthetic materials. Here we are still faced with the task of a huge organized research effort. It consists primarily in a rational distribution of the work between academic institutes, industrial institutes and plant laboratories. Some institutes are far removed from industry, are not sufficiently acquainted with its needs and problems, and frequently operate without the necessary contact with those departments of institutes that work on the engineering and technological aspects of new processes.

It should be acknowledged that we still lack a sufficiently broad front of new research studies, assuring the creation of a reservoir of scientific knowledge, which is necessary especially in such a field as new synthetic materials. It is imperative that a large portion of the scientists, operating in academic institutes, devote their research efforts to seeking new methods that will facilitate the best execution of the enormous tasks presently confronting Soviet chemists.

The Soviet people should be assured of having at their disposal various types of fabrics made from artificial and synthetic fibers, artificial leather and fur, not only of a high quality but also much cheaper than the natural. The building and furniture industries should receive durable and (attractive) handsome materials based on synthetic polymers. Here a broad field of activity opens up for research in the fields of the chemistry of high-molecular compounds, organic synthesis and catalysis, physical chemistry, and the physics of solids and crystals. The problem of creating artificial materials with certain given properties has to be solved. Advances in the chemistry of high-molecular compounds, the latest achievements in the field of theoretical organic chemistry, the radiation chemistry of polymers, the successfully worked-out methods of effective graft and block copolymerization and the synthesis of oriented polymers will all partially help in the solution of this problem. Its solution should also be facilitated by conducting theoretical studies in the field of the chemistry of heteroorganic compounds, and by the synthesis of polymers based on these compounds, containing in their composition silicon, fluorine, phosphorus, various metals, and other elements.

An energetic development of the chemistry of high-molecular compounds will permit a constantly increasing replacement of empirical directions for the preparation of plastics and other high-molecular materials by strictly scientific rules. Theoretical studies on the development of new and improved technological processes will also be expanded. We should create highly efficient and economically feasible methods for the processing of both natural and petroleum by-product gases, of petroleum, of coal, and of various plant wastes, which would permit obtaining raw materials for the synthesis of polymeric materials, and we should also create commercial methods for the preparation and processing of polymers.

A new branch of chemical science, namely radiation chemistry, will receive special attention in the forthcoming seven-year plan. It is also proposed to expand the studies pertaining to the chemistry and technology of the rare elements, the importance of which in the national economy rises sharply in proportion to expansion in the research investigations directed to a study of their properties and to a search for new fields of their application. Technical progress in atomic energetics and in the metallurgical, aviation, machine-construction, chemical, radiotechnical and optical industries depends to a large degree on the assured availability of the rare elements in sufficient amounts.

Devoting their forces first of all to a solution of actual scientific problems, having paramount importance for the national economy, both research institutes and higher educational institutions should arrive at a point where scientific problems are worked out exhaustively and in an encompassing manner where the investigations are quickly brought to a close, and where the investigations results are introduced without delay into industry. An end must be put to the practice where individual workers and laboratories in some scientific institutions labor for a long time without showing serious research productivity.

The majestic plan for the future development of the national economy in the USSR during 1959-1965 confronts the scientists with some great tasks. There is no doubt but that Soviet scientists will fulfill these tasks.

POLAROGRAPHIC BEHAVIOR OF METAL IONS IN THE SYSTEM
FORMIC ACID-WATER

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Polarographic studies in mixed solvents are of great theoretical interest, since various physicochemical transformations, progressing in the studied media, can affect the electroreduction of ions. The use of binary liquid systems as solvents in the polarographic study of the reduction of metal ions, especially in the case where chemical reaction between the components of the system is postulated, should give some valuable information regarding the physicochemical nature of the studied medium. The purpose of the present investigation was to study the effect of the composition of a mixed solvent on the polarographic characteristics (in particular, on the diffusion current) of simple metal ions, and to use the obtained data to construct the phase diagrams. We selected the system formic acid-water as the mixed solvent.

A study of the physicochemical properties of the system $HCOOH-H_2O$ was made by A. A. Glagoleva. She studied the viscosity [1], electroconductivity [2], surface tension [3], density [4] and fusibility [5] of the indicated binary system.

Analysis of the isotherms of the system made it possible to establish the presence and composition of two hydrates in the system, and specifically $HCOOH \cdot H_2O$ and $HCOOH \cdot 2H_2O$.

As was shown by N. A. Izmailov and V. D. Bezuglyi [6], a change in the value of the diffusion current in going from water to a nonaqueous solvent can be due to a change in the viscosity, size of the particles being reduced, concentration of the substance being reduced, pH, etc. The relationship, derived from the Ilkovic and Stokes-Einstein equations [7], is usually used in discussing the effect of solvent viscosity on polarographic diffusion currents:

$$K_s \eta^{1/3} = \text{const}, \tag{1}$$

where: $K_s = i_d/c$ is the diffusion-current constant, and η is the viscosity of the solvent.

It was shown by A. M. Zan'ko and F. A. Manusova [8] that the nature of the solvent exerts great influence on the polarographic diffusion current. They found that the height of the Cd^{++} wave in the system formamide — water passes through a maximum when the formamide is diluted. The authors explain this anomalous change in the value of i_d as due to a change in the nature of the solvent itself as the result of reaction between formamide and water.

Other authors [9-11] also found that an aqueous alcohol solvent exerts substantial influence on the value of the polarographic diffusion current of ions of the alkali and alkaline earth metals when the alcohol concentration is varied from 0 to 100% They associate the minimum, found at 80% alcohol, with supersolvation of the ions.

EXPERIMENTAL

The polarographic properties of the ions Cd^{++}, Zn^{++} and Pb^{++} were studied in aqueous formic acid medium. We used 0.1 M KCl solution as the "indifferent" electrolyte in the polarographing of Cd^{++} and Zn^{++} The polarographing of Pb^{++} was run without an "indifferent" electrolyte using an aqueous solution of the acid as the support.

Fig. 1. Relationship between the diffusion current and the concentration of cadmium ions.
HCOOH concentration (in %):
1) 5;   2) 17; 3) 32; 4) 66; 5) 86;
6) 100.

Fig. 2. Relationship between the diffusion current and the concentration of zinc ions.
HCOOH concentration (in %):
1) 10; 2) 17; 3) 24; 4) 32;
5) 42; 6) 53.

The aqueous formic acid solvent was prepared from anhydrous HCOOH, which was prepared using the method described by Lange [12].   The purity of the acid was controlled by the specific electroconductivity and the density. The formic acid used by us had the following constants: $\kappa = 7.5 \cdot 10^{-5}\,ohm^{-1} \cdot cm^{-1}$. The polarographing was run in acid ranging in concentration from 0 to 100%.   We investigated 6-7 metal-ion concentrations in the interval 0.2 to 0.9 mmole/liter, in each mixed solvent. The same capillary with the characteristics $m^{2/3}\, t^{1/6} = 1.82$ $mg^{2/3} \cdot sec^{-1/2}$, was used in all of the experiments. The calomel electrode, saturated in 75% HCOOH, served as the reference electrode. The polarographic cell used in the study was built along the lines of the Maassen apparatus [7]. The investigated solution was separated from the reference electrode by a glass filter. The polarographic cell was kept in a thermostat at $25 \pm 0.2°$. Dissolved oxygen was removed by blowing with nitrogen. Blowing for up to 1.5 hours was required in the case of high oxygen concentrations. The nitrogen was first passed through a corresponding solution, where it became saturated with acid and water vapors.

To run the experiments we used a homemade polarographic apparatus with a mirror galvanometer having a sensitivity of $1.44 \cdot 10^{-9}$ amp/mm. The accuracy of measuring the potentials was $\pm$ 0.005 v. Depending on the composition of the solvent, the resistance of the polarographic cell ranged from approximately 1000 to 8000-10,000 ohms.

Taking into consideration the ohmic drop of the voltage in the polarographic cell, a correction was made for all of the points on the polarographic curve, after which the corresponding slope coefficients of the straight lines were found from the plots $\varphi - \log \dfrac{i}{i_d - i}$.
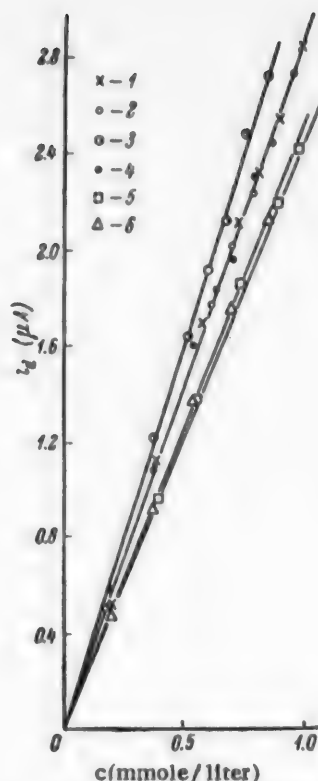
Fig. 3. Relationship between the diffusion current and the concentration of lead ions. HCOOH concentration (in %): 1) 5; 2) 10; 3) 32; 4) 59; 5) 82; 6) 100.

Distinct polarographic waves for the metal ions were obtained in both aqueous formic acid solvents and anhydrous formic acid, even in the absence of an "indifferent" electrolyte. In contrast to aqueous solutions, the polarographing of Zn^{++} and Pb^{++} in water — formic acid medium was not accompanied by the appearance of maxima on the volt — ampere curves, which is explained by the powerful surface-active properties of formic acid.

The relationships between the diffusion current and the metal ion concentration are shown in Figs. 1 — 3. As can be seen from these graphs, a proportionality between the strength of the diffusion current and the metal-ion concentration are shown in Figs. 1 — 3. As can be seen from these graphs, a proportionality between the strength of the diffusion current and the metal-ion concentration exists at all of the concentrations investigated. Here the diffusion-current constant K_s changes substantially with change in the acid concentration, as is obvious from the data given in the table and plotted in Figs. 4 — 6. The error in measuring K_s was 2 — 3%.

The slope coefficients of the straight lines $\varphi - \log \dfrac{1}{I_d - 1}$, found for Cd^{++}, Zn^{++} and Pb^{++} in water–forming acid solutions, lie close to the theoretical values, which is evidence that the reduction process is reversible.

From Figs. 4 and 6 it can be seen that the change in the values of the diffusion-current constants for Cd^{++} and Pb^{++} with increase in the acid concentration is accompanied by the appearance of two distinct maxima at an acid concentration of 30 and 50 mole %. In polarographing Zn^{++} it proved impossible to investigate the region of acid concentrations above 50 mole % due to the superimposition of the hydrogen ion wave, but, as can be seen from Fig. 5, the change in the diffusion current constants of Zn^{++} is also accompanied by the appearance of a maximum in the region of 30–40 mole % acid. This change in K_s is undoubtedly associated with the formation of hydrated complexes of the acid, having one and two molecules of water, and, respectively, corresponding to 33 and 50 mole %HCOOH.
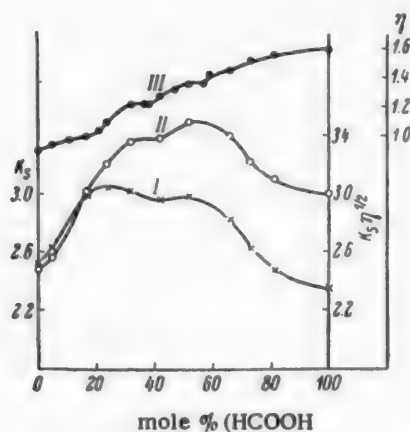
Fig. 4. Diagram of solvent composition vs diffusion-current constant of cadmium ions. I) K_s; II) $K_s \eta^{1/2}$; III) η.
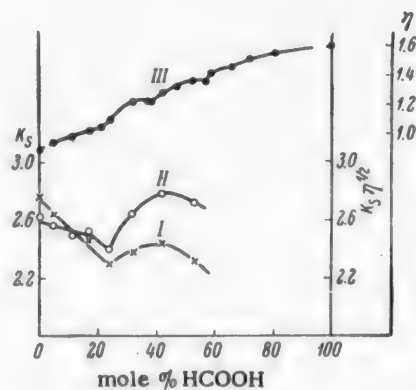
Fig. 5. Diagram of solvent composition vs diffusion-current constant of zinc ions. I) K_s, II) $K_s \eta^{1/2}$; III) η.

Polarographic Characteristics of Cd^{++}, Zn^{++} and Pb^{++} in the System $HCOOH-H_2O$

Mole % HCOOH	Cd^{++}			Zn^{++}			Pb^{++}		
	K_s	$\varphi_{1/2}$	slope coefficient of the straight line $\varphi-\lg\frac{i}{i_d-i}$	K_s	$\varphi_{1/2}$	slope coefficient of the straight line $\varphi-\lg\frac{i}{i_d-i}$	K_s	$\varphi_{1/2}$	slope coefficient of the straight line $\varphi-\lg\frac{i}{i_d-i}$
0	2.52	0.54	0.030	2.76	0.96	0.030	—	—	—
5	2.63	0.53	0.028	2.64	0 92	0.031	2.90	0.30	0.026
10	—	—	—	2.52	0.90	0.031	2.90	0.32	0.029
17	2.95	0.51	0.028	2.48	0.89	0.030	2.84	0.30	0.026
24	3.04	0.49	0.029	2.29	0.87	0.030	2.74	0.29	0.028
32	3.02	0.48	0.027	2.38	0.85	0.032	3.18	0.28	0.027
42	2.96	0.47	0.030	2.44	0.83	0.030	2.93	0.27	0.029
53	2.99	0.46	0.032	2.52	0.82	0.034	2.93	0.24	0.026
59	—	—	—	—	—	—	2.86	0.23	0.029
68	2.81	0.45	0.031	—	—	—	2.64	0.22	0.026
73	2.62	0.45	0.035	—	—	—	—	—	—
82	2.48	0.44	0.030	—	—	—	2.50	0.19	0.028
100	2.37	0.43	0.033	—	—	—	2,47	0.17	
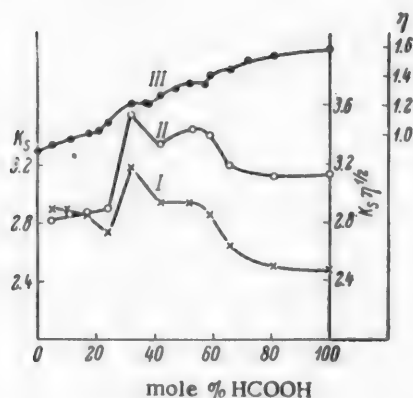
Fig. 6. Diagram of solvent composition vs diffusion current constant of lead ions. I) K_s; II) $K_s \, \eta^{1/2}$; III) η.

The maxima for the diffusion-current constants, appearing in the interval of acid concentrations corresponding to the formation of hydrated complexes, are evidently linked with a change in the solution structure, which leads to a reduction in the dimensions of the solvate shell of the ion. A reduction in ion dimensions facilitates its more rapid movement to the electrode surface and, consequently, an increase in the diffusion current.

The magnitude of the diffusion current depends mainly on D — the diffusion coefficient of the ion. A change in the diffusion coefficient may be due to both a change in the dimensions of the solvate shells of the ions and a change in the viscosity of the solvent. In this connection we used the Ilkovic-Stokes-Einstein equation (1) to correct the diffusion current constants for viscosity. The viscosity values used were taken from [1]. Results are plotted in Figs. 4—6. The maxima on the $K_s \, \eta^{1/2}$ — solvent composition curves are expressed as clearly as on the K_s — solvent composition curves. This indicates that supersolvation of the ions plays the major role in increasing diffusion current constant values in the region of acid concentrations corresponding to the hydrate's composition although the viscosity curves also indicate that two hydrates are present.

SUMMARY

1. The polarographic characteristics of the ions Cd^{++}, Zn^{++} and Pb^{++} in the system $HCOOH-H_2O$ were studied.

2. The plots of diffusion-current constant vs solvent composition were obtained. It was shown that the change in the diffusion-current constants as a function of solvent composition is accompanied by the appearance of two maxima in the concentration interval corresponding to the composition of the mono- and dihydrates of the acid, which is in accord with the curves for the viscosity, electroconductivity, and other studied properties of the system $HCOOH-H_2O$.

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POLAROGRAPHIC BEHAVIOR OF METAL IONS IN THE SYSTEM
ACETIC ACID-WATER

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In the previous paper [1] we had studied the behavior of the ions Cd^{++}, Zn^{++} and Pb^{++} in the system formic acid-water. The present paper is devoted to a study of the influence exerted by the composition of water-acetic acid solvents on the polarographic diffusion current of simple metal ions.

A detailed study of the physicochemical properties of the system $CH_3COOH-H_2O$ was made by A. A. Glagoleva. She studied the viscosity [2], electroconductivity [3], density [4] and surface tension [5] of the indicated system. These studies revealed that the system $CH_3COOH-H_2O$ is an irrational one, since both maxima and minima, characterizing the formation of hydrated complexes with composition $CH_3COOH \cdot H_2O$ and $CH_3COOH \cdot 2H_2O$, were found to be present on the isotherms of all of the studied physicochemical properties in a certain region of acid concentration.

EXPERIMENTAL

The cations Cd^{++}, Zn^{++} and Ni^{++} were subjected to polarographic reduction. We used 0.01 M NH_4NO_3 solution as the indifferent electrolyte. The aqueous acetic acid solvent was prepared from anhydrous CH_3COOH and double-distilled water. The acid used in our experiments had the following constants: b.p. $118°$, m.p. $16°$, d_4^{25} 1.049. The polarographing was run in the acid-concentration range of 0 to 80 mole %. Six concentrations of metal ion were investigated in each mixed solvent in the interval of 0.2 to 1 mmole/liter. The reference electrode was a saturated calomel electrode. The measurements were made at $25 \pm 0.2°$.

The polarographic cell, method of oxygen removal and characteristics of the capillary have been described earlier [1].

In finding the true values of the half-wave potentials and in verifying the reversible nature of the electroreduction process by the method of plotting the graphs of φ vs log $\frac{i}{i_d - i}$ we made a correction for the voltage drop in the polarographic cell due to ohmic resistance. Distinct polarograms for the ions Cd^{++}, Zn^{++} and Ni^{++} were obtained in all of the mixed solvents investigated. In contrast to water solutions, the polarographing of Zn^{++} and Ni^{++} in water-acetic acid medium was not accompanied by the appearance of maxima on the volt - ampere curves, which is explained by the powerful surface-active properties of acetic acid.

The measurement results are given in the table; the relationship between the diffusion current and the metal-ion concentration is shown in Fig. 1-3. As can be seen from these graphs, a proportionality between i_d and C was observed in the investigated interval of acid concentration (0-80 mole %). The error in measuring K_s was 2-3%.

The slope coefficients of the straight lines φ vs log $\frac{i}{i_d - i}$ for the ions Cd^{++} and Zn^{++} in acetic acid solutions practically coincide with the theoretical value $(2.3 \frac{RT}{nF})$, which indicates the reversible nature of the electroreduction process; for the ion Ni^{++}, which reduces irreversibly in water medium, the electroreduction process approaches the reversible one in the acid concentration range of 10 to 50 mole %.
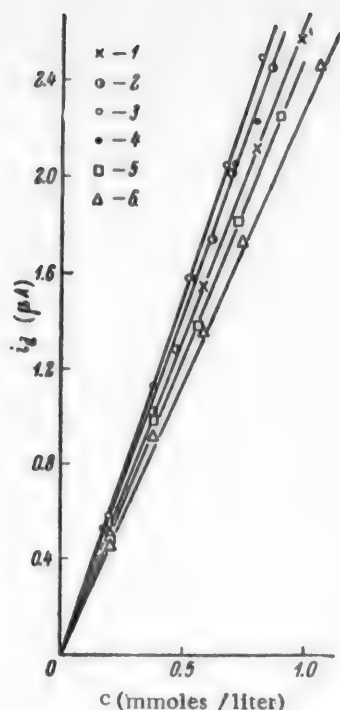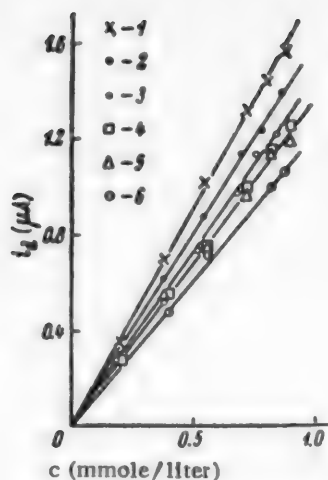
Fig. 1. Relationship between the diffusion current and the concentration of cadmium ions.
CH_3COOH concentration (in %):
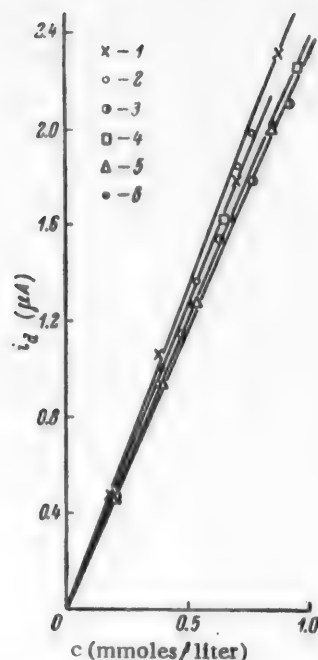1) 7; 2) 24; 3) 36; 4) 49; 5) 63; 6) 74.

Fig. 2. Relationship between the diffusion current and the concentration of zinc ions.
CH_3COOH concentration (in %):
1) 7; 2) 24; 3) 42; 4) 56; 5) 63; 6) 74.
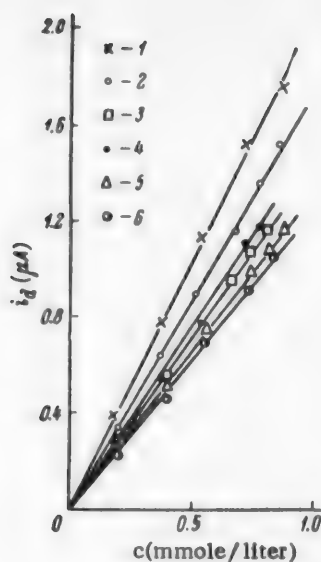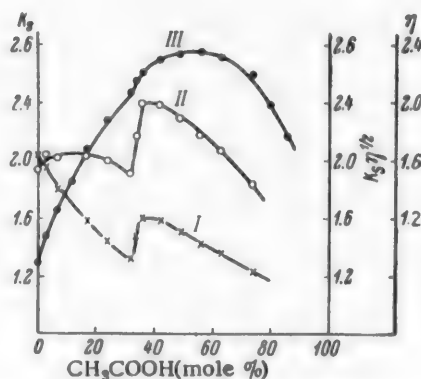
Fig. 3. Relationship between the diffusion current and the concentration of nickel ions.
CH_3COOH concentration (in %):
1) 7; 2) 17; 3) 32; 4) 42; 5) 56; 6) 63.

Fig. 4. Diagram of solvent composition vs diffusion-current constant of cadmium ions.
I) K_s; II) $K_s \eta^{1/2}$; III) η.

From Figs. 4-6 it can be seen that the change in the diffusion current constants K_s of the indicated metal ions with increase in the acid concentration was accompanied by the appearance of distinct inflection points in the interval of 33 to 50 mole % acid. It is obvious that this change in K_s, the same as in the case of the polarographing of metal ions in the system $HCOOH-H_2O$ [1], is connected with supersolvation of the ions, which in turn depends on the chemical reaction between the components.

Since the change in the diffusion-current constants in going from a water solvent to a mixed one may be

due to a change in both the dimensions of the solvate shells of the ions and the viscosity of the solvent, we used the Ilkovic-Stokes-Einstein equation $K_s \eta^{1/2}$ = const [6] to make suitable correction for the viscosity. This equation is valid only if a change in viscosity is the only reason for a change in the value of the diffusion current constant.
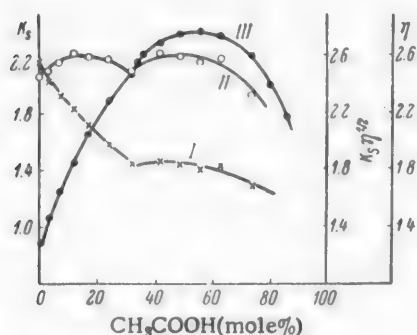
Fig. 5. Diagram of solvent composition vs diffusion-current constant of zinc ions.
I) K_s; II) $K_s \eta^{1/2}$; III) η.
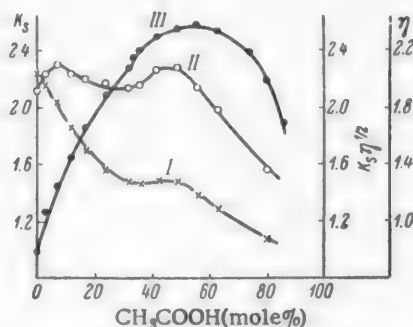
Fig. 6. Diagram of solvent composition vs diffusion-current constant of nickel ions.
I) K_s; II) $K_s \eta^{1/2}$; III) η.

Polarographic Characteristics of Cd^{++}, Zn^{++} and Ni^{++} in the System $CH_3COOH-H_2O$

mmoles

CH₃COOH (mole %)	Cd^{++}			Zn^{++}			Ni^{++}		
	K_s $\mu A/\frac{mM}{liter}$	$\varphi^{1/2}$ V	slope coefficient of straight line $\varphi - \lg \frac{i}{i_d - i}$	K_s $\mu A/\frac{mM}{liter}$	$\varphi^{1/2}$ V	slope coefficient of straight line $\varphi - \lg \frac{i}{i_d - i}$	K_s $\mu A/\frac{mM}{liter}$	$\varphi^{1/2}$ V	slope coefficient of straight line $\varphi - \lg \frac{i}{i_d - i}$
0	2.04	0.575	0.0304	2.17	1.00	0.0309	2.24	0.966	0.0514
3.4	1.97	0.570	0.0288	2.02	0.978	0.0290	2.16	0.987	0.0514
7.0	1.80	0.575	0.0305	1.93	0.970	0.0288	2.05	0.967	0.0440
12.0	—	—	—	1.84	0.962	0.0323	1.85	0.965	0.0394
17.0	1.58	0.530	0.0327	1.71	0.955	0.0328	1.70	0.964	0.0494
24.0	1.45	0.524	0.0293	1.58	0.930	0.0266	1.56	0.940	0.0410
32.0	1.32	0.509	0.0298	1.45	0.917	0.0312	1.48	0.925	0.0424
34.0	1.48	0.526	0.0302	—	—	—	—	—	—
36.0	1.61	0.495	0.0307	—	—	—	1.45	0.920	0.0420
42.0	1.57	0.484	0.0282	1.46	0.883	0.0291	1.48	0.903	0.0377
49.0	1.50	0.492	0.0355	1.44	0.870	0.0320	1.48	0.895	0.0416
56.0	1.42	0.476	0.0300	1.40	0.847	0.0285	1.38	0.877	0.0520
63	1.36	0.463	0.0270	1.43	0.820	0.0321	1.29	0.857	0.0556
74	1.23	0.430	—	1.29	0.802	0.0285	—	—	—
80	—	—	—	—	—	—	1.09	0.766	0.0660

From Figs. 4-6 it can be seen that in the indicated mixed solvent, $K_s \eta^{1/2}$ = const (the values of η were taken from [2]) for all of the metal ions investigated. From this it follows that not the viscosity, but instead the change in the size of the solvate shells of the ions, i.e. the supersolvation process, is predominantly responsible for the change in the diffusion-current constants of metal ions in the system $CH_3COOH-H_2O$.

SUMMARY

1. The polarographic characteristics of the ions Cd^{++}, Zn^{++} and Ni^{++} in the system $CH_3COOH-H_2O$ were studied.

2. The plots of diffusion-current constant vs solvent composition were obtained. It was shown that the change in the diffusion-current constants as a function of solvent composition is accompanied by the appearance of distinct inflection points in the interval of acid concentrations corresponding to the formation of hydrated complexes.

3. The Ilkovic-Stokes-Einstein equation was used to suitably correct the diffusion-current constant for the viscosity. An examination of the $K_s \eta^{1/2}$ − solvent composition curves reveals that the change in K_s with increase in the acid concentration is mainly due to supersolvation of the ions.

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COORDINATION COMPOUNDS OF ZIRCONIUM TETRACHLORIDE
WITH ESTERS OF MONOBASIC ACIDS. XV.

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In our previous communication [1], devoted to complex compounds of zirconium tetrachloride with esters of monobasic acids, it was shown that the formation of complexes of the type $ZrCl_4 \cdot 2RCOOR_1$ is accompanied by enhanced polar properties. The zirconium in such complex compounds possesses the coordination number most characteristic for it, namely six. According to Sidgwick [2], zirconium can have a coordination number of 5, 6, 7 or 8 in its complexes. In the present investigation our task was to determine if complexes exist in which zirconium has its minimum coordination number of five. For this purpose we investigated compounds having the composition $ZrCl_4 \cdot RCOOR_1$, both preparatively and based on their cryoscopic and polar properties in benzene solution. The methods used to determine the dipole moments and the molecular weights cryoscopically, and also the purification of the compounds used in the study, have been described by us earlier [1, 3, 4].

RESULTS AND DISCUSSION

According to Blumenthal [5], zirconium tetrachloride is insoluble in such nonpolar solvents as benzene, carbon tetrachloride, carbon disulfide and titanium tetrachloride. Actually, when zirconium tetrachloride was shaken for a long time (more than 100 hours) with benzene we were unable to detect even traces of dissolved $ZrCl_4$ in the latter. When $ZrCl_4$ is shaken with benzene in the presence of an equimolar amount of an ester, the zirconium chloride dissolves completely. With a smaller amount of the ester in benzene the excess $ZrCl_4$ remains undissolved even after very long shaking. This fact serves as evidence that complex compounds, having the composition $ZrCl_4 \cdot RCOOR_1$, are formed in benzene solutions containing equimolar amounts of $ZrCl_4$ and ester. *

As we will see below, the complex $ZrCl_4 \cdot RCOOR_1$ shows coordination unsaturation and for this reason can easily add still another molecule of an oxygen-, sulfur- or nitrogen-containing addendum with the formation of a mixed complex $ZrCl_4 \cdot RCOOR_1 \cdot A$, where A is the addendum molecule.

The results of measuring the dielectric permeability (ϵ) and the density (d), and also the calculated values of of the polarization (P_2), of complexes of $ZrCl_4$ with one mole of ethyl formate, isopropyl formate, ethyl acetate, isopropyl acetate or ethyl butyrate, as a function of the mole fraction of the corresponding complex, are given in Tables 1-5. The obtained data show that complexes with the composition $ZrCl_4 \cdot RCOOR_1$ possess a substantial dipole moment. The increase in the dipole moment at the $Zr-O$ bond (Table 6) is approximately 1.8-2.2 debyes. Here it should be mentioned that the magnitude of the dipole moment decreases with increase in the molecular weight of the ester, which is in agreement with earlier studies [1,4] The character of the relationship between the polarization of complexes with composition $ZrCl_4 \cdot RCOOR_1$ and the concentration is evidence that these complexes have a great tendency to associate even at large dilution.

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*Here the discussion pertains to solutions of low concentration, where the uncomplexed portion of the $ZrCl_4$ cannot dissolve in the benzene due to the presence of the complex $ZrCl_4 \cdot 2RCOOR_1$ in solution.

TABLE 1

Complex $ZrCl_4 \cdot HCOOC_2H_5$ in C_6H_6
$P_\infty = 420$ cm^3, R = 56.65 cm^3, $\mu = 4.15$ D

c (mole fraction)	ε_{20}	d_4^{20}	P_2
0.00183	2.329	0.8815	362
0.00246	2.340	0.8827	346
0.00359	2.358	0.8848	323
0.00515	2.382	0.8876	306
0.00678	2.412	0.8908	305
0.00958	2.464	0.8960	304
0.01581	2.575	0.9068	299

TABLE 2

Complex $ZrCl_4 \cdot HCOOC_3H_7$ in C_6H_6
$P_\infty = 430$ cm^3, R = 59.10 cm^3, $\mu = 4.18$ D

c (mole fraction)	ε_{20}	d_4^{20}	P_2
0.00192	2.328	0.8819	340
0.00286	2.339	0.8835	303
0.00382	2.348	0.8852	275
0.00480	2.359	0.8869	263
0.00622	2.377	0.8894	256
0.00876	2.409	0.8937	250
0.01470	2.492	0.9042	249

TABLE 3

Complex $ZrCl_4 \cdot CH_3COOC_2H_5$ in C_6H_6
$P_\infty = 384$ cm^3, R = 60.09 cm^3, $\mu = 3.89$ D

c (mole fraction)	ε_{20}	d_4^{20}	P_2
0.00186	2.323	0.8818	309
0.00246	2.328	0.8829	288
0.00311	2.336	0.8841	265
0.00411	2.342	0.8859	271
0.00507	2.349	0.8876	222
0.00661	2.359	0.8902	214
0.00921	2.386	0.8947	213
0.01540	2.455	0.9054	210

TABLE 4

Complex $ZrCl_4 \cdot CH_3COOC_3H_7$ in C_6H_6
$P_\infty = 380$ cm^3, R = 62.41 cm^3, $\mu = 3.85$ D

c (mole fraction)	ε_{21}	d_4^{20}	P_2
0.00183	2.320	0.8816	300
0.00220	2.324	0.8823	286
0.00307	2.332	0.8857	260
0.00376	2.336	0.8850	238
0.00540	2.358	0.8895	215
0.00886	2.384	0.8936	215
0.01333	2.431	0.9012	213

TABLE 5

Complex $ZrCl_4$ $C_3H_7COOC_2H_5$ in C_6H_6
$P_\infty = 340$ cm^3, R = 70.19 cm^3, $\mu = 3.53$ D

c (mole fraction)	ε_{20}	d_4^{20}	P_2
0.00191	2.315	0.8820	254
0.00268	2.321	0.8834	231
0.00389	2.329	0.8856	209
0.00564	2.342	0.8887	197
0.00712	2.357	0.8915	199
0.01031	2.385	0.8970	197
0.01710	2.450	0.9092	195

TABLE 6

Complex	μ	μ_1	$\mu - \mu_1$
$ZrCl_4 \cdot HCOOC_2H_5$	4.15	1.92	2.23
$ZrCl_4 \cdot HCOOC_3H_7$	4.18	1.89	2.28
$ZrCl_4 \cdot CH_3COOC_2H_5$	3.89	1.81	2.08
$ZrCl_4 \cdot CH_3COOC_3H_7$	3.85	1.85	2.00
$ZrCl_4 \cdot C_3H_7COOC_2H_5$	3.53	1.74	1.79

As can be seen from the presented data (Tables 1-5), at concentrations exceeding 0.005 mole fraction of complex in benzene, the curves expressing the polarization as a function of the concentration $[P_2 = f (C)]$ pass nearly parallel to the abscissa, and it is only at concentrations below 0.005 that polarization increases, indicating decomposition of the associated molecules.

To confirm the above we determined the molecular weight of the complexes in benzene cryoscopically. These results are given in Tables 7-11.

TABLE 7

Molecular Weight of Complex $ZrCl_4$ $HCOOC_2H_5$

C(mole fraction)	$\Delta t°$	Mdetd.	$\alpha = \dfrac{M\text{detd.}}{M\text{theoret.}}$
0.0145	0.454	650	2.12
0.0119	0.374	646	2.11
0.00929	0.294	638	2.08
0.00653	0.207	635	2.07
0.00435	0.140	624	2.03
0.00231	0.081	573	1.87

TABLE 8

Molecular Weight of Complex $ZrCl_4 \cdot$ $\cdot HCOOC_3H_7$

C(mole fraction)	$\Delta t°$	Mdetd.	$\alpha = \dfrac{M\text{detd.}}{M\text{theoret.}}$
0.0136	0.433	668	2.08
0.0109	0.348	665	2.07
0.00870	0.279	658	2.05
0.00685	0.220	658	2.05
0.00463	0.151	646	2.01
0.00267	0.095	590	1.84

TABLE 9

Molecular Weight of Complex $ZrCl_4 \cdot$ $\cdot CH_3COOC_2H_5$.

C (mole fractions)	$\Delta t°$	Mdetd.	$\alpha = \dfrac{M\text{detd.}}{M\text{theoret.}}$
0.0159	0.519	653	2.03
0.0123	0.398	655	2.04
0.00901	0.289	659	2.05
0.00661	0.216	646	2.01
0.00402	0.133	635	1.98
0.00265	0.092	606	1.83

TABLE 10

Molecular Weight of Complex $ZrCl_4$ $\cdot CH_3COOC_3H_7$

C (mole fractions)	$\Delta t°$	Mdetd.	$\alpha = \dfrac{M\text{detd.}}{M\text{theoret.}}$
0.0149	0.499	663	1.98
0.0120	0.397	670	2.00
0.00918	0.304	666	1.99
0.00681	0.223	673	2.01
0.00442	0.147	660	1.97
0.00281	0.097	634	1.89

TABLE 11

Molecular Weight of Complex $ZrCl_4 \cdot$ $\cdot C_3H_7COOC_2H_5$

C (mole fractions)	$\Delta t°$	Mdetd.	$\alpha = \dfrac{M\text{detd.}}{M\text{theoret.}}$
0.0145	0.454	650	2.12
0.0119	0.374	646	2.11
0.00929	0.294	638	2.08
0.00653	0.207	635	2.07
0.00435	0.140	624	2.03
0.00231	0.081	573	1.87

The freezing point of each solution was taken as the average of three determinations (the differences did not exceed 0.002°). For convenience in comparing the cryoscopic data with the polarization results for the same complexes, the concentrations in all cases are expressed in mole fractions.

The results given above for a determination of the molecular weight clearly indicate that the investigated complexes show a great tendency to associate even at very high dilution. The complex $ZrCl_4$ $RCOOR_1$ is found as the dimer in dilute benzene solutions, i.e. equilibrium in the reaction

$$2ZrCl_4 \cdot RCOOR_1 \rightleftarrows [ZrCl_4 \cdot RCOOR_1]_2$$

is almost completely shifted to the right. It must be assumed that this great tendency to dimerize at high dilution is not due to a simple dipole interaction of the complex $ZrCl_4 \cdot RCOOR_1$ molecules, possessing substantial polarity, but instead is due to their coordination unsaturation. Such a dimer should have a clawlike structure, in which zirconium has a coordination number of six.
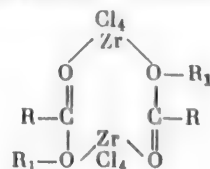
The dimer molecule cannot have a planar structure, since in such case its dipole moment would be equal to zero, which is contradictory to the experimental data.

To obtain the above complex compounds we isolated them from saturated benzene solutions (with the exception of the complex $ZrCl_4 \cdot HCOOC_2H_5$). The complexes were obtained as follows: an accurately weighed amount of zirconium tetrachloride and a small amount of benzene (2-3 ml per gram of zirconium tetrachloride) were placed in a glass ampul, and then the proper ester was added in an amount strictly equivalent to the taken $ZrCl_4$. The ampuls were sealed and fastened to a revolving disk. Crystals of the complex began to deposit from solution as the $ZrCl_4$ went into solution. The ampuls had to be shaken for about 50-60 hours to obtain complete reaction, after which the ampul contents were transferred to a glass filter. The filtration was done in a special container, through which a stream of well-dried air was passed during the whole experiment. In addition, the filter funnel was connected to a drier, through which previously dried air was also passed until the crystals of the complex were completely dry. The thus-obtained complexes $ZrCl_4 \cdot CH_3COOC_2H_5$, $ZrCl_4 \cdot CH_3COOC_3H_7$ and $ZrCl_4 \cdot C_3H_7COOC_2H_5$ were analyzed, the results of which are given in Table 12. The melting points of the obtained complexes, and also those of the complexes formed from titanium tetrachloride and the corresponding esters [6], are also given in Table 12. As can be seen, the melting points of the titanium complexes are considerably below those of the analogous zirconium complexes. We will mention that the isolated $ZrCl_4$ complexes were obtained as fine, colorless, needle crystals, readily hydrolyzing in moist air. We took carbon tetrachloride as the solvent to obtain the complex $ZrCl_4 \cdot HCOOC_2H_5$, since this complex, when isolated from benzene solutions, had quite a different appearance from the other zirconium complexes. Here the crystals were coarse and on long drying they were converted to a powder. Analysis of the thus-obtained compound for chlorine and zirconium revealed that both of these elements were present in considerably smaller amount than that required for the complex with composition $ZrCl_4 \cdot HCOOC_2H_5$, and instead the compound corresponds to the complex $ZrCl_4 \cdot HCOOC_2H_5 \quad C_6H_6$. When the latter complex was dissolved in water we

TABLE 12

Complex	Chlorine		Zirconium		Melting point	Melting point of the corresponding $TiCl_4$ complex
	found	calculated	found	calculated		
$ZrCl_4 \cdot CH_3COOC_2H_5$	0.439	0.443	0.286	0.284	170°	102°
$ZrCl_4 \cdot CH_3COOC_3H_7$	0.423	0.424	0.276	0.272	129	78
$ZrCl_4 \cdot C_3H_7COOC_2H_5$	0.404	0.407	0.262	0.261	163	103
$ZrCl_4 \cdot HCOOC_2H_5$	0.455	0.463	0.299	0.297	94	56

obtained a completely clear water solution, containing the ester and the $ZrCl_4$ hydrolysis products, and also a small amount of an upper layer, having a benzene odor. Investigation of this upper layer revealed that it was mainly benzene, present in amount equivalent to the complex with composition $ZrCl_4 \quad HCOOC_2H_5 \cdot C_6H_5$, which melts without decomposition at 54°. To determine the strength of the bond between benzene and zirconium tetrachloride in this complex, we heated the complex to 90° in a special vessel in a steady stream of dry air. Here the loss in the weight of the complex was checked at periodic intervals by accurate weighing. It proved that after 120 minutes (at 90°) the weight of the complex corresponded to the composition $ZrCl_4 \cdot HCOOC_2H_5$, i.e. the benzene had completely volatilized. This was also confirmed by analyzing for zirconium and chlorine. A similar complex, containing toluene instead of benzene, was obtained by the long shaking of $ZrCl_4$ with toluene, the latter containing ethyl formate in an amount equivalent to the zirconium tetrachloride taken. The analysis results for chlorine, zirconium and toluene corresponded to the compound with composition $ZrCl_4 \cdot HCOOC_2H_5 \cdot C_7H_8$, having m.p. 50°.

Data indicating that the tetrahalides of Group IV elements react with aromatic hydrocarbons exist in the literature [7, 8]. The fact that aromatic hydrocarbons possess π-electrons is the reason for the formation of such addition products. That this postulation is true is supported by the absence of reaction between cyclic paraffins and the halides of Group IV elements. However, we will mention that we were unable to find similar information for the zirconium halides in the literature available to us. Despite this, complexes of the type

$ZrCl_4 \cdot HCOOC_2H_5 \cdot C_6H_6$ could be of considerable interest in studying the catalytic effect of $ZrCl_4$ in organic synthesis. It is quite probable that $ZrCl_4$ gives similar mixed complexes also with other esters of monobasic acids, but in them the benzene is linked very weakly and is rapidly cleaved at ordinary temperatures. Thus, we observed that when $ZrCl_4$ was shaken with an equivalent amount of propyl acetate in benzene at a temperature below $+15°$, it was not fine needle crystals, characteristic for complexes with the composition $ZrCl_4 \cdot RCOOR_1$, that were formed, but instead they were quite coarse crystals, resembling the crystals of the complex $ZrCl_4 \cdot$ $\cdot HCOOC_2H_5 \cdot C_6H_6$. However, these coarse crystals decomposed at 20-25°, changing to fine needle crystals. Based on preliminary results, zirconium bromide also forms a complex in which benzene is present. These investigations are being continued by us.

SUMMARY

1. We isolated and analyzed the complexes $ZrCl_4 \cdot HCOOC_2H_5$, $ZrCl_4 \cdot HCOOC_3H_7$, $ZrCl_4 \cdot CH_3COOC_2H_5$, $ZrCl_4 \cdot CH_3COOC_3H_7$ and $ZrCl_4 \cdot C_3H_7COOC_2H_5$, and determined their dipole moments in benzene. It was shown that the dipole moment of the complex decreases with increase in the molecular weight of the ester component.

2. The cryoscopic method was used to determine the molecular weights of the above complexes. It was shown that all of these complexes display a great tendency to associate. Some reasons for this association were postulated.

The ternary complexes

$$ZrCl_4 \cdot HCOOC_2H_5 \cdot C_6H_6 \quad \text{and} \quad ZrCl_4 \cdot HCOOC_2H_5 \cdot C_6H_5CH_3$$

were isolated and analyzed, and their melting points were determined.

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THE REDUCTION OF FURFURAL AT A DROPPING-MERCURY ELECTRODE

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The great importance of furfural in industry creates the need for more accurate methods of its quantitative determination, among which the polarographic method is finding constantly broader use. In this connection, a study of the polarographic reduction of furfural seems of interest, all the more so since contradictory data exist on the matter.

I. A. Korshunov and S. A. Ermolaeva [1] investigated the reduction of furfural at a dropping-mercury electrode in buffer solutions ranging in pH from 4.0 to 7.25. The buffer mixtures used by them were composed of acetic acid and sodium acetate, and also of citric acid and dibasic sodium phosphate. These buffer mixtures had concentration of about 0.1 N. One wave was observed at pH 4, and the half-wave potential was equal to 1.24 v (with reference to the saturated calomel electrode). Two waves were observed in the pH range from 5.5 to 6.5, in which connection the height of the first wave decreased, and that of the second wave increased, as the pH increased. With increase in the pH the potential of the first half-wave shifts to the negative side, while that of the second half-wave shifts to the positive side. Only one wave was observed at pH 7.25, and here the half-wave potential (π) was equal to -1.7 v.

Day [2] considers Korshunov's results as being questionable both on the score of the two-step reduction of furfural and the values of the half-wave potential, pointing out that Tachi, who polarographed a 0.0001 M furfural solution in buffer mixtures with different pH values, observed only one wave, in which connection the half-wave potentials were more positive than those given in Korshunov's studies.

We were unable to obtain the original paper by Tachi, published in a Japanese journal. However, the data of Tachi are given in the monograph by I. M. Kolthoff and J. J. Lingane [3], according to which the half-wave potential of furfural shifts to the negative side as the pH rises from 1.1 to 11.0, going from 0.93 to -1.47 v. The half-wave potential (-1.47 v) reached at pH 11.0 does not change with further increase in the pH.

The value of the furfural diffusion current depends on the pH. The diffusion current reaches its highest value at pH 8.0.

Day polarographed a 0.001 M furfural solution in 25% alcohol in buffer mixtures ranging in pH from 1.0 to 13.0 and obtained the following results. Two waves with nearly the same height were obtained only at pH 5.0. At pH values below 4.0 the height of the wave was hardly one half that of the wave at pH 6.0-7.0. The values of the half-wave potentials did not differ from those given in Tachi's studies. Day believes the reason for the unusual behavior shown by furfural in Korshunov's studies is an insufficient buffering of the solutions.

We think that the different, and in some cases even contradictory, results obtained by Tachi, Korshunov, and Day are due to the polarographing of furfural under different conditions. Korshunov, using various buffer mixtures, does not differentiate the polarographic waves and half-wave potentials obtained by him as a function of the composition of the buffer mixtures used. Korshunov in his paper does not give the furfural and alcohol concentrations at which the polarographing was run, whereas this is important in determining the values of the diffusion current and the half-wave potential. Kolthoff and Lingane do not state the nature of either the buffer mixtures or the solution used by Tachi in his polarographing of furfural. Day in his paper also does not indicate the nature of the buffer mixtures or the concentration of the alcohol used by him in the polarographing of furfural.

In the present paper we set ourselves the task of studying the gradation of the reduction, the value of the diffusion current and the value of the half-wave potential of furfural as functions of whether a water or a water-alcohol medium is used, the composition of the buffer mixture, and the pH.

EXPERIMENTAL

Alcohol-Water Solutions

Furfural, b.p. 161-162°, was polarographed in both water and water-alcohol solutions. The ethyl alcohol concentration in the water-alcohol solutions used was 30, 40 and 60%.

For the polarographing we used an automatic polarograph of the SGM-8 type; the galvanometer sensitivity was $3.3 \cdot 10^{-9}$ amp/mm. The time of mercury dropping was 2.3-2.35 sec. The removal of oxygen from the solutions was effected by adding several drops of saturated sodium sulfite solution. We used 0.1 N ammonium chloride as the support. The volume ratio of studied solution to support was 1:1, i.e. the concentrations of furfural, alcohol and support in the electrolyzer were cut in half. The obtained results are given in Table 1.

TABLE 1

Values of Diffusion Current (i) and Half-Wave Potential (π) of Furfural

(t = 2.3 sec; C = 50 mg/liter; s = 1/15)

Solvent	i (in mm on the galvanometer scale)	π relative to the saturated calomel electrode
Water	34.8	−1.4
15 % alcohol. . . .	24.8	−1.5
20% alcohol	22.6	−1.6
30% alcohol	18.8	−1.7

From the data in Table 1 it can be seen that the value of the diffusion current of furfural is smaller in water-alcohol solutions than in water solution. The value of the diffusion current decreases with increase in the alcohol concentration. This is explained by a decrease in the diffusion coefficient (D) due to an increase in the viscosity of the solution when the alcohol concentration is increased. (The other terms, found in the Ilkovic equation $i_d = 605 n D^{\frac{1}{2}} C m^{\frac{2}{3}} t^{\frac{1}{6}}$, and specifically: n — the number of electrons participating in the reduction reaction, C — the furfural concentration, and also the product $m^{\frac{2}{3}} t^{\frac{1}{6}}$ do not change with change in the solvent composition)

In going from water to a water-alcohol solvent, the half-wave potential shifts to the negative side. The values of this potential become more negative the higher the alcohol concentration. It must be assumed that the reason for the half-wave potential of furfural changing in a water-alcohol medium when compared with pure water is due to a change in the dielectric constant of the solvent.

Consequently, the alcohol concentration affects the value of both the diffusion current and the half-wave potential of furfural. This was not taken into consideration in the above-mentioned studies, which is one of the reasons for the contradictory results.

Buffer Mixtures

A water solution of furfural (C = 50 mg/liter) was polarographed. As the support we used 0.1 N buffer mixtures with a variable pH. To remove oxygen we passed hydrogen through the investigated solution for 30 minutes prior to polarographing.

As buffer mixtures we used: a) acetate buffer solutions with pH ranging from 3.6 to 5.3, b) citric acid-phosphate buffer solutions with pH ranging from 3.6 to 7.4, and c) phosphate buffer solutions with pH ranging from 3.6 to 5.3,   b) citric acid-phosphate buffer solutions with pH ranging from 3.6 to 7.4, and c) phosphate buffer solutions with pH ranging from 6 to 7.4.

The results are given in Table 2.

TABLE 2

Values of Diffusion Current (i) and Half-Wave Potential (π) as Functions of the Buffer Mixture Composition and the pH;   C = 50 mg/liter, $\leq$ 1/30, t = 3 sec

pH of the me-dium	Buffer mixtures											
	$Na_2HPO_4+C_6H_8O_7$				$CH_3COOH+CH_3COONa$				$Na_2HPO_4+NaH_2PO_4$			
	i_1 (mm)	π_1 (V)	i_2 (mm)	π_2 (V)	i_1 (mm)	π_1 (V)	i_2 (mm)	π_2 (V)	i_1 (mm)	π_1 (V)	i_2 (mm)	π_2 (V)
3.6	22	1.19	—	—	24	1.21	—	—	—	—	—	—
4.3	21	1.25	21	1.4	21	1.24	23	1.46	—	—	—	—
4.6	22	1.24	20	1.4	20	1.25	25	1.42	—	—	—	—
5.0	19	1.24	20	1.40	20	1.33	22	1.47	—	—	—	—
5.3	19	1.31	21	1.55	22	1.4	22	1.55	—	—	—	—
6.0	—	—	41	1.40	—	—	—	—	—	—	41	1.4
6.8			50	1.45	—	—	—	—	—	—	51	1.5
7.4			52	1.5	—	—	—	—	—	—	54	1.6

From the data in Table 2 it can be seen that two waves are observed at pH 4.3, 4.6, 5.0 and 5.3 in both the citric acid-phosphate and the acetate buffers. Only one wave is obtained at all of the other pH values.

Consequently, the two-step reduction of furfural observed in the studies of Korshunov and Ermolaeva is confirmed, to be sure, not in the pH interval 5.5-6.5, but instead in the pH interval 4.3-5.3. The height of the wave at pH 3.6 is nearly one half that of the wave at pH 6, which is in agreement with Day's observations. In the pH range 4.3-5.3, the sum of the heights of the two waves in the acetate buffer varies between 42-45 mm and is somewhat greater than the sum of the heights of these waves in citric acid-phosphate buffer (39-42 mm). A noticeable increase in the diffusion current is observed at pH 6.8-7.4. In phosphate buffer mixture the height of the wave is equal to 51-54 mm and differs but slightly from the same wave in citric acid-phosphate buffer (50-52 mm), which, as can be seen, is due to the component Na_2HPO_4 being common to both of the indicated buffer solutions. The potential of the first half-wave of furfural tends to shift to the negative side as the pH increases. The half-wave potentials in the acetate and phosphate buffers are more negative than in the citric acid-phosphate buffer.

Consequently, not only the pH, but also the composition of the buffer mixture affects the values of both the diffusion current and the half-wave potential, which Day does not take into consideration when comparing Korshunov's results with those obtained by Tachi.

SUMMARY

It was shown that the reduction of furfural at a mercury-dropping cathode is two step in a certain pH range.

Both the pH and the composition of the buffer mixture affect the values of the diffusion current and the half-wave potential of furfural.

In this connection only one distinct polarographic wave is obtained in all cases at pH > 7, making it possible to measure the value of the diffusion current and to conveniently run the polarographic quantitative determination of furfural in alkaline medium, all the more so since sodium sulfite can be used to remove oxygen from such a medium.

The value of the diffusion current of furfural is smaller, and the value of the half-wave potential is more negative, in a water-alcohol medium than in water solutions. The wave height decreases as the alcohol concentration is increased, while the absolute value of the half-wave potential increases.

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THE REACTION OF MOLYBDATE AND VANADATE WITH PHENOLS
IN WATER SOLUTIONS AND IN CONCENTRATED SULFURIC ACID

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Vanadium and molybdenum form colored compounds with certain phenols in water solutions and in concentrated sulfuric acid. Different phenols are used as reagents in the colorimetric determinations of vanadate and molybdate [1,2].

With the exception of Levy's studies [3], where the colors of the solutions in concentrated sulfuric acid are described, we failed to find any papers in the literature devoted to a discussion of the problems associated with the reaction of vanadium (5+) and molybdenum (6+) with hydroxy compounds. Consequently it seemed of interest to us to investigate some of the problems pertaining to the indicated reactions.

REACTION IN WATER SOLUTIONS

Color of a Solution and its Dependence on the pH.

We studied the reaction of vanadium and molybdenum salts with a number of aromatic hydroxy compounds: phenol, pyrocatechol, resorcinol, hydroquinone, pyrogallol, phloroglucinol, α- and β-naphthols, thymol and gallic acid.   The purity of the organic reagents was checked by their melting points. The solutions of ammonium vanadate and molybdate were prepared from c.p. reagents, recrystallized from ammonia. For the experiments we mixed 1 ml of a 0.001 M solution of ammonium vanadate or ammonium molybdate with 1 ml of a 0.1 M solution of the phenol in the presence of 8 ml of a buffer solution, the pH of the latter ranging from 1 to 10 (mixtures of HCl + KCl were used for the 1-2 pH range, and acetate-ammonia mixtures for the 3-10 pH range). The different solutions were mixed, and after 10 minutes their color was observed visually, while the optical density value was measured using a FEK-M photocolorimeter in cuvettes with a layer thickness of 10 mm, and using a blue filter transmitting light in the 400-500 mμ region. To check the acidity of the solutions after reaction we used a pH-meter of the LP-5 type with a glass electrode. It was observed that only pyrocatechol, pyrogallol and gallic acid, i.e. only those phenols having either two OH groups or an OH and a COOH ortho to each other, form highly colored solutions with salts of vanadium (5^+) and molybdenum (6^+). The other hydroxy compounds investigated (phenol, resorcinol, hydroquinone, phloroglucinol, α- and β-naphthols, thymol)failed to give colored reaction products. The experimental data are given in Table 1 and plotted in   Figs. 1 and 2.

An examination of the data given in Table 1 and plotted in Fig. 1 reveals that pyrocatechol pyrogallol and gallic acid form colored compounds with molybdenum that are very similar, both as regards their color and the intensity of the color. The color becomes noticeable even at pH 1, and reaches its optimum value at pH 6-9.

A similarity in color is not observed for the compounds of vanadate with phenols (Table 1, Fig. 2), while the relationship between the optical density and the pH is different than for the molybdate compounds. Thus, when vanadate solutions are reacted with pyrocatechol or gallic acid a sharp increase in the optical density is observed in the 2-6 pH range; with further increase in the pH the optical density diminishes, assuming for the compound of vanadate with gallic acid a constant value at pH 8-10. When the vanadate is reacted with pyrogallol the optical density of the colored solution rises sharply in the 2-4 pH range, remaining constant at pH 4-8.5; the optical density diminishes with further increase in the pH.

Reaction of vanadate and molybdate with phenols. From the literature it is known that in many cases the reactions of metals with phenols yield compounds in which one or several of the hydrogen atoms in the phenol is replaced by the metal ion [1, 4-6]. An increase in the H-ion concentration is observed in such case. If the reaction goes without the liberation of hydrogen ions, then addition products of the phenol with the complexing ion are formed.

To determine the character of the reactions taking place when pyrocatechol, pyrogallol and gallic acid are reacted with molybdate and vanadate ions, we performed the following experiments: 10 ml of a 0.1M solution of the salt was mixed with 10 ml of a 0.5 M solution of the phenol, and after 5 minutes the pH of the mixture was measured potentiometrically, using an LP-5 bulb potentiometer with glass electrode. The pH's of the phenol and salt solutions were measured in advance. The concentration of the reactants in the reaction mixture is cut in half when the phenol and salt solutions are mixed. By itself, this dilution has very little effect on the acidity of the reactant solution. Thus, when 0.1M solutions of ammonium molybdate and ammonium vanadate are diluted in half, the pH drops by 0.15-0.20, while when the phenols are diluted in half, the pH of the solutions increases by 0.30. The results of measuring the pH of the solutions before and after mixing are given in Table 2.
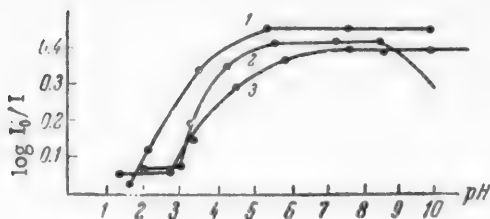
Fig. 1. Relationship between the optical density of solutions containing ammonium molybdate and a phenol, and the pH.
1) gallic acid, 2) pyrogallol, 3) pyrocatechol

From the data in Table 2 it follows that the acidity of the solutions rose substantially when the molybdate was reacted with phenols (the only exception to this was the mixture of molybdate with gallic acid, where the acidity increased very slightly). When compared with the original pH values of the phenols, the acidity of the solutions does not increase when the vanadate is reacted with phenols.

Since both ammonium molybdate and ammonium vanadate had pH values considerably above those of the phenols, then it was possible for reaction to occur even with an increase in the H-ion concentration, which remained unobserved because the acidity of the mixtures was always somewhat less than the acidity of the phenol solutions. For this reason we ran some additional experiments by a different method: the acidity of the salt solutions was brought to the acidity of the phenol solutions with hydrochloric acid, after which the solutions were mixed, and the pH measured after 5 minutes. The data of these experiments are given in Table 3.

Fig. 2. Relationship between the optical density of solutions, containing ammonium vanadate and a phenol, and the pH.
1) gallic acid, 2) pyrogallol, 3) pyrocatechol.

Consequently, molybdenum salts with pyrocatechol, pyrogallol and gallic acid form inner complexes, in which the metal ions displace the hydrogen ions from the phenols; the vanadate apparently forms addition products with the indicated phenols.

Reaction of vanadate and molybdate with phenols in concentrated sulfuric acid. Levy [3], who studied the reaction of some organic reagents with titanic, tantalic, stannic, vanadic, molybdic, arsenous and arsenic acids, states that many phenols give bright colors with the indicated acids in concentrated sulfuric acid. Since Levy was very vague in describing the experimental conditions used by him (several crystals of the investigated substance were taken for experiment), we studied the reaction of ammonium vanadate and ammonium molybdate with the above phenols in the following manner: 0.5 ml of a 0.01 M solutions of ammonium vanadate or ammonium molybdate was mixed with 0.5 ml of an equimolar solution of the phenol, after which the mixture was made up to 15 ml, using concentrated sulfuric acid in one case, and concentrated hydrochloric acid in the other. The colors that were obtained in this manner are given in Table 4.

TABLE 1

Color of Solutions as a Function of the pH

pH	Ammonium vanadate			Ammonium molybdate		
	pyrocatechol	pyrogallol	gallic acid	pyrocatechol	pyrogallol	gallic acid
0.9	Light pink	Orange	Light yellow	Pale yellow	Pale yellow	Yellow
2.4	Likewise	Likewise	Yellow	Yellow	Yellow-orange	Orange
3.1	"	Brown-orange	Pale green	Likewise	Likewise	Likewise
4.9	Yellow	Green	Yellow-green	Orange	"	"
5.6	Likewise	Likewise	Likewise	Red	Orange	"
6.3	Yellow-brown	Brown-green	"	Likewise	Likewise	"
8.3	Likewise	Orange-brown	"	"	"	"
9.2	"	Likewise	"	"	"	"
10.3	"	"	Green	"	Brown-orange	Brown

TABLE 2

pH of Pure Solutions

0.5 M Solutions of phenols	pH	0.1 M Solutions of salts	pH
Pyrocatechol	3.92	Ammonium molybdate	5.48
Pyrogallol	3.98	Ammonium vanadate	7.75
Gallic acid	2.70		

pH of Mixtures

Salts / Phenol	0.1 M Ammonium molybdate, 10 ml	0.1 M Ammonium vanadate, 10 ml
0.5 M Pyrocatechol, 10 ml	2.82	4.60
0.5 M Pyrogallol, 10 ml	3.04	4.65
0.5 M Gallic acid, 10 ml	2.50	4.00

TABLE 3

pH of Mixtures of Phenols with Salts

Salts / Phenol	Ammonium molybdate	Ammonium vanadate
Pyrocatechol	1.90	4.00
Pyrogallol	2.00	3.86
Gallic acid	1.50	2.70

It should be mentioned that the colors of the compounds change widely depending on the concentrations of the metals and reactants. The colored solutions show a high sensitivity. We made a study of some of their physicochemical properties. The optical density was determined as being the most characteristic property of such systems.

TABLE 4

Colors of Compounds in Concentrated Sulfuric and Hydrochloric Acids
(our data)

Phenols	Ammonium vanadate		Ammonium molybdate	
	H_2SO_4	HCl	H_2SO_4	HCl
Pyrocatechol	Light yellow-green	Light yellow	Emerald green	Colorless
Resorcinol	Pale brown-yellow	Light pink	Pink-orange, blue-violet	Colorless
Hydroquinone	Emerald green	Light yellow	Emerald green	Likewise
Pyrogallol	Brown-red	Likewise	Dark brown	Light violet
α-Naphthol	Emerald green	Light blue with opal-escence	Emerald green	Colorless
β-Naphthol	Brown	Colorless	Colorless	Likewise
Gallic acid	Light Brown	Orange-red	Likewise	"
Chromotropic acid	Colorless	Colorless	"	"

SPECTROPHOTOMETRIC STUDY OF THE RELATIONSHIP BETWEEN COLOR AND THE SULFURIC ACID CONCENTRATION, EXCESS OF REAGENT, AND THE TIME

Relationship Between Optical Density and the Sulfuric Acid Concentration

In studying the color reactions of titanium with phenols in concentrated sulfuric acid, one of us established the relationship existing between the optical density of colored solutions and the acidity [7]. By means of preliminary experiments it was established that in the case of molybdate — and vanadate — phenol solutions the optical density is even more dependent on the acidity. The study was made as follows: a $3.3 \cdot 10^{-4}$M solution of either ammonium molybdate or vanadate was mixed in a ground-glass stoppered glass cylinder with a definite excess of the phenol in 80% H_2SO_4 solution, after which sulfuric acid of variable concentration was added. The total volume of each mixture was 15 ml. The various mixtures were then thoroughly mixed, and their optical densities measured at the end of definite time intervals (15 min, 30, min, 1 hr, 4 hrs, and 24 hrs), using cuvettes, a layer thickness of 10 mm, and light-filters with the optimum wave-length characteristics. The curves for the light absorption of the mixtures are shown in Figs. 3 and 4.

The shape of the curves indicates that the color intensity is a strongly dependent on the sulfuric acid concentration, in which connection the highest intensity is reached in 95% sulfuric acid.

Relationship Between Optical Density and Excess of Reagent and Time of Reaction

Based on preliminary experiments it was established that the optical density of the colored solutions depends on the molar ratio of hydroxy compound to either vanadate or molybdate. To establish the optimum excess of reagent we took 0.5 ml aliquots of a 0.01 M solution of either vanadate or molybdate and mixed them with various amounts of a 0.1 M solution of the hydroxy compound. Each mixture was then diluted with concentrated sulfuric acid to a total volume of 15 ml. The optical density of the colored solutions was measured 15 minutes after mixing, using a FEK-M- photocolorimeter and a blue light filter with λ_{max} 420 mμ (the only exceptions were the solutions of molybdate and vanadate with α-naphthol, where the optical density was measured
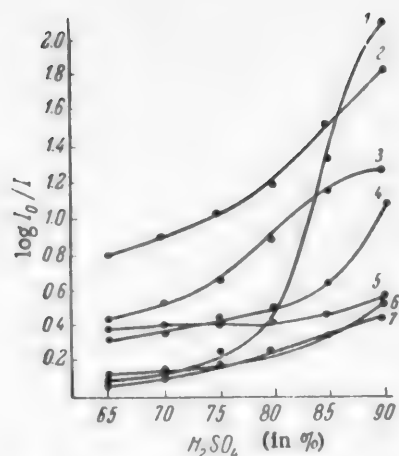
Fig. 3. Relationship between the optical density of solutions and the percent content of sulfuric acid for solutions of vanadate with various phenols.
1) hydroquinone, 2) pyrocatechol, 3) resorcinol, 4) pyrogallol, 5) gallic acid, 6) α-naphthol, 7) β-naphthol.

Fig. 4. Relationship between the optical density of solutions and the percent content of sulfuric acid for solutions of molybdate with various phenols.
1) hydroquinone, 2) resorcinol, 3) pyrogallol, 4) α-naphthol.

using a red light filter with λ_{max} 570 mμ and the solution of vanadate with β-naphthol, where the optical density was measured using a green light filter with λ_{max} 530 mμ in cuvettes with a layer thickness of 10 mm). The experimental data are plotted in Figs. 5 and 6. From the curves it can be seen that the optical density as a function of the molar ratios increases differently for the different phenols, whereas for the mixtures of vanadate with resorcinol, pyrogallol, α-naphthol and β-naphthol the maximum optical density is reached with a 3-fold excess of the reagent; for the compound of vanadate with tallic acid it is not reached even with a 60-fold excess of the latter.

A reduction in the optical density after reaching the optical maximum is observed for most of the colored solutions, and in a number of cases a change in the color when further excess reagent is added. This indicates the possible formation of several complexes. The color becomes stabilized in 10-15 minutes, and then the optical density does not change with time.

DETERMINATION OF THE COMPOSITION OF THE COLORED COMPOUNDS OF VANADIUM AND MOLYBDENUM WITH PHENOLS IN CONCENTRATED SULFURIC ACID

The method of isomolar series in 90% sulfuric acid was used by us to determine the ratios of the reacting components in colored solutions. * For this, 0.01 M solutions of vanadate and molybdate were mixed with equimolar solutions of a number of phenols in such manner that the total volume of each mixture was 1 ml. Then 14 ml of concentrated sulfuric acid was added to each mixture. To determine the change in the optical density as a function of the molar ratio, we used a FEK-M photocolorimeter, and the measurements were made at the end of 15 minutes, 1 hour, and 2 hours, using cuvettes, a layer thickness of 10 mm, and light-filters with the optimum wavelengths. The experimental data are shown in Figs. 7 and 8, where the concentrations of the components in the mixtures are plotted along the abscissa, and the optical densities are plotted along the ordinate (in the case of colored solutions for the components it is the deviation of the optical density from additivity that is plotted along the ordinate). The results of these experiments indicate that vanadate forms compounds of the 2:3 type with hydroquinone, resorcinol, and pyrogallol, of the 1:1 type with pyrocatechol and α-naphthol, and of the 2:1 type with β-naphthol.

In the case of molybdate a compound of the 3:2 type is formed with α-naphthol, of the 2:3 type with pyrogallol, of the 1:2 type with hydroquinone, and of the 1:4 type with pyrocatechol.

*The state of vanadium (5+) and molybdenum (6+) ions in acid medium depends to a large degree on the acid concentration. Most authors assume that VO^{3+} is formed in strongly acid medium [8-10]. In a recent paper by Chauveau [11] pertaining to molybdenum, it is stated that MoO_2Cl_2 is formed in concentrated hydrochloric acid, and that the complex $[MoO_3 \cdot SO_4 \cdot H_2]H^+$ is formed in sulfuric acid when the concentration ranges from 1.5 to 8 M. We failed to find data in the literature on the character of the molybdate complex in more concentrated sulfuric acid.

Fig. 5. Relationship between the optical density and the molar ratios of phenol: vanadate and phenol: molybdate.

1) hydroquinone: molybdate, 2) pyrocatechol: : vanadate, 3) hydroquinone: vanadate, 4) resorcinol: vanadate, 5) pyrogallol: molybdate, 6) α-naphthol: molybdate, 7) α-naphthol: : vanadate, 8) β-naphthol: vanadate.

Fig. 6. Relationship between the optical density and the molar ratios of phenol : vanadate and phenol: molybdate.

1) resorcinol: molybdate, 2) pyrogallol: vanadate, 3) gallic acid: vanadate.

Fig. 7. Composition of vanadate-phenol compounds in concentrated sulfuric acid. 1) pyrocatechol, 2) pyrogallol, 3) hydroquinone, 4) resorcinol, 5) β-naphthol, 6) α-naphthol.
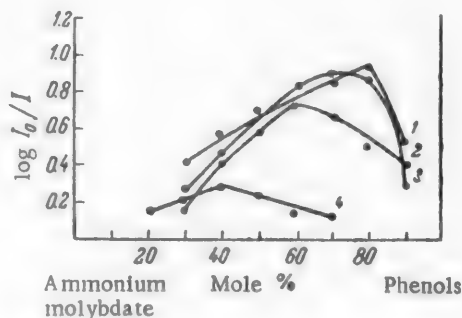
Fig. 8. Composition of molybdate-phenol compounds in concentrated sulfuric acid. 1) pyrocatechol, 2) pyrogallol, 3) hydroquinone, 4) α-naphthol.

SUMMARY

1. Vanadates and molybdates form intensely co-lored solutions at pH 4-10 with only those hydroxy compounds in which the complex-forming groups stand ortho to each other. However, in concentrated sulfuric acid they form colored solutions with many phenols, independent of the structure of the latter.

2. The color of the compounds depends to a large degree on the excess of reagent, and in strongly acid solutions, also on the sulfuric acid concentration. The optimum color is obtained in concentrated sulfuric acid. Dilution of the sulfuric acid leads to a sharp decrease in the color intensity. It is difficult to select the threshold (interval) of sulfuric acid concentrations in which the color remains stable. The fact that the solution color depends on the molar ratio of hydroxy compound to vanadate or molybdate indicates the possible formation of a number of complexes.

The character of the reaction of vanadate and molybdate with phenols in weakly acid medium was determined, as was also the composition of the compounds formed in concentrated sulfuric acid.

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LIQUID-CRYSTAL EQUILIBRIUM IN SYSTEMS INVOLVING FLUORANTHENE

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Recently we had published some study results on the equilibria existing between the liquid and crystalline phases in systems involving the four-ring hydrocarbons, pyrene [1] and chrysene [2]. Data only partially characterizing some of the phase diagrams of fluoranthene are reported in a paper by Frank (he fails to give any information as to when crystallization ends in the systems)[3].

Fig. 1. Liquid-crystals equilibrium in systems of fluoranthene with benzene (1), durene (2), naphthalene (3), 2-methyl-naphthalene (4), 2,7-dimethylnaphthalene (5),phenanthrene (6),fluorene (7),anthracene (8), and acenaphthene (9).

In this communication we discuss that group of systems involving fluoranthene that are considered as being the quantitatively predominant components of coal tar. We studied nine binary systems, in which the second components were benzene, 1,2,4,5-tetramethylbenzene (durene), naphthalene, 2-methylnaphthalene, 2,7-dimethylnaphthalene, phenanthrene, fluorene, anthracene and acenaphthene, i.e. representatives of one-, two- and three-ring aromatic hydrocarbons.

EXPERIMENTAL

System components. For our work we took "pure" compounds, labeled as being of highest quality and m.p., and purified them further, either by distillation or recrystallization, after which they had the following melting points: benzene 5.48-5.51°, durene 79.0-79.2°, naphthalene 80.0-80.2°, 2-methylnaphthalene 34.0-34.1°, 2,7-dimethylnaphthalene 97.0°, phenanthrene 99.2-99.4°, fluorene 114.0-114.2°, anthracene 216.5°, and acenaphthene 95.0-95.2°.

Method used to study the phase equilibria. The thermal analysis method was used to obtain all the experimental data, supplemented by visual observations. An electromagnetic stirrer was used to stir the melts. Details of both the method and the apparatus have been described earlier [4].

Binary Systems of Fluoranthene

As was revealed by the experiments in which the temperature of the start and end of crystallization for mixtures with a variable content of components was determined, all nine systems involving fluoranthene belong to the eutectic type. The numerical data, characterizing the conditions of phase equilibria in the individual systems, are given in the summary table; the phase diagrams constructed from these data are shown in Fig. 1.

Binary Systems of Fluoranthene with Aromatic Hydrocarbons.

Fluoranthene concentration		Crystallization temperature		Fluoranthene concentration		Crystallization temperature	
wt.%	mole %	start	eutectic	wt.%	mole %	start	eutectic

1. Fluoranthene — Benzene / 2. Fluoranthene — Durene

wt.%	mole %	start	eutectic	wt.%	mole %	start	eutectic
100.00	100.0	110.0°	..	100.00	100.0	110.0°	—
71.22	48.9	75.1	—	91.85	88.2	101.6	58.5°
66.23	43.1	70.1	—	84.42	78.2	95.0	58.6
58.20	34.9	60.0	..	73.61	64.9	85.0	59.0
50.99	28.6	51.2	-	63.71	53.8	76.0	59.0
42.30	22.0	42.6	—	55.00	44.8	67.2	59.0
37.40	18.7	36.3	1.0°	50.02	39.9	61.3	59.0
34.80	17.1	34.5	1.1	48.14	38.2	59.0	59.0
30.37	14.4	27.6	1.2	44.76	35.0	59.5	59.0
26.63	12.3	22.3	1.2	37.54	28.5	63.3	59
22.70	10.2	17.0	1.2	32.00	23.8	66.2	59
17.59	7.6	7.7	1.2	22.37	16.0	70.1	58.8
15.31	6.5	4.0	1.2	12.26	8.5	74.2	58.8
13.67	5.7	1.2	1.2	0.00	0.0	79.2	—
10.78	4.4	1.7	1.2				
4.80	2.1	3.3	1.2				
0.00	0.0	5.5	-				

3. Fluoranthene — Naphthalene / 4. Fluoranthene — 2-methyl-naphthalene

wt.%	mole %	start	eutectic	wt.%	mole %	start	eutectic
				100.0	100.0	110.0°	...
				92.65	89.8	102.4	—
100.00	100.0	110.0°	—	81.67	75.8	91.9	18.6°
91.75	87.5	101.0	55.4°	73.09	65.6	83.4	18.8
72.90	70.7	88.2	55.6	66.31	58.0	76.5	19.0
71.59	61.4	79.6	55.6	57.83	49.2	68.1	19.0
63.0	54.9	70.3	55.7	50.00	41.4	57.1	19.2
57.40	46.1	63.9	55.8	42.13	33.8	44.2	19.0
52.40	41.1	57.7	55.8	36.56	28.9	37.0	19.2
50.15	39.0	55.8	55.8	30.50	23.6	24.7	19.0
44.52	33.7	59.0	55.8	26.33	20.1	19.3	19.3
34.12	24.7	65.3	55.7	22.00	16.5	20.6	19.3
17.31	11.7	73.1	55.4	17.34	12.9	23.3	19.3
0.00	0.0	80.2	—	13.78	10.1	25.2	19.3
				0.00	0.0	34.1	—

5. Fluoranthene — 2,7-Dimethyl-naphthalene / 6. Fluoranthene — Phenanthrene

wt.%	mole %	start	eutectic	wt.%	mole %	start	eutectic
100.00	100.0	110.0°	—	100.00	100.0	110.0°	...
89.15	86.4	99.4	—	90.75	89.6	102.5	-
80.20	75.8	90.6	65.8°	76.20	73.8	91.8	—
72.64	67.2	83.2	65.8	67.32	64.4	85.3	72.8°
65.28	59.3	76.1	66.0	59.60	56.3	80.2	72.8
57.32	50.9	67.5	66.0	51.15	48.0	74.3	72.8
54.70	48.2	66.0	66.0	49.17	46.0	73.0	73.0
46.42	42.8	71.0	66.0	42.10	39.1	76.4	72.8
35.21	29.6	79.4	65.9	32.10	29.4	82.1	—
25.31	20.8	84.9	65.7	17.36	15.6	90.6	–
10.62	8.4	92.1	65.6	7.26	6.5	95.5	—
0.00	0.0	97.0	—	0.00	0.0	99.3	—

7. Fluoranthene — Fluorene / 8. Fluoranthene — Anthracene

wt.%	mole %	start	eutectic	wt.%	mole %	start	eutectic
100.00	100.0	110.0°	—	100.00	100.0	110.0°	—
92.06	90.5	103.1	68.7°	93.78	93.0	104.6	—
82.73	79.7	94.9	68.7	91.60	90.6	103.3	101°
74.40	70.4	86.8	68.8	89.59	88.4	101.8	101
67.02	62.5	79.4	69.0	88.40	86.0	101.0	101
61.83	57.1	74.7	69.0	87.37	85.9	107.0	101
57.86	53.0	69.9	69.0	85.48	83.0	114.1	101

Binary Systems of Fluoranthene with Aromatic Hydrocarbons

Fluoranthene concentration		Crystallization temperature		Fluoranthene concentration		Crystallization temperature	
wt. %	mole %	start	eutectic	wt. %	mole %	start	eutectic
7. Fluoranthene —Fluorene				8. Fluoranthene—Anthracene			
56.74	51.9	69.0	69.0	82.26	80.4	122.5	101
52.00	47.7	72.1	69.0	69.86	67.1	146.7	100.8
43.00	38.9	80.6	69.0	59.62	56.6	162.0	100.6
34.10	29.8	90.5	68.8	48.71	45.6	176.2	100.4
22.78	19.5	100.0	68.8	38.50	35.5	186.5	100.3
11.85	9.9	107.5	68.7	29.44	26.9	194.2	100.0
0.00	0.0	114.0	--	19.82	17.8	201.9	99.7
				0.00	0.0	216.5	..
9.Fluoranthene —Acenaphthene							
100.00	100.0	110.0		49.63	42.9	62.1°	61.8
85.21	81.5	95.6		45.45	38.8	66.2	61.8
79.73	75.2	90.2	61.6	35.19	29.3	75.0	61.7
66.82	60.6	77.5	61.8	20.35	16.3	84.9	61.5
55.95	49.2	67.6	61.8	10.51	9.2	89.1	61.3
50.58	43.8	61.8	61.8	0.00	0.0	95.1	

1. System fluoranthene-benzene. The eutectic contains 13.67 wt.% (5.7 mole %) of fluoranthene; it crystallizes at 1.2°; the latter value was confirmed by second eutectic rests on the thermal-analysis curves in all of the studied mixtures. On the diagram of state that portion of he curve corresponding to 80-110° is plotted as a dotted line, since the corresponding mixtures, having a benzene content of less than 28% by weight, were not studied at temperatures above the boilining point of benzene at atmospheric pressure. However, this did not impede the conclusion that the phase equilibria in the system fluoranthene-benzene are of the eutectic type. Both components crystallized from vigorously stirred melts when the degree of supercooling did not exceed 1-2°.

2. System fluoranthene- 1,2,4,5-tetramethylbenzene (durene). The eutectic crystallizes at 59.0° and has a fluoranthene content of 48.14 wt.% (38.2 mole %). In all of the experiments second eutectic rests were observed on all of the thermal analysis curves at 59-58.5°. In the crystallization of fluoranthene from stirred melts, the supercooling did not exceed 2-3°, while the durene crystals deposited from the melt almost immediately.

3. Systems fluoranthene-naphthalene. The eutectic mixture contains 50.15 wt.% (39.0 mole %) of fluoranthene; the eutectic temperature is 55.8°; the latter value was excellently confirmed by second rests on the thermal-analysis curves of all of the studied mixtures. The components crystallized from the stirred melts with very slight supercooling (1-2°).

4. System fluoranthene—2-methylnaphthalene. The eutectic mixture contains 26.33 wt.% (20.1 mole %) fluoranthene. It crystallizes at 19.3°. The supercooling in the crystallization of fluoranthene from stirred melts was 1-3°, and in the crystallization of 2-methylnaphthalene it was 3-6°.

5. System fluoranthene—2,7-dimethylnaphthalene. The eutectic-point coordinates are: 66.0° and fluoranthene content 54.70 wt.% (48.2 mole %). The supercooling in the crystallization of the components from stirred melts is 2-4°.

6. System fluoranthene-phenanthrene. Here the fluoranthene concentration in the eutectic mixture is 49.17 wt.% (46.0 mole %), and the eutectic temperature is 73.0°. In the experiments here it was revealed that second eutectic rests on the thermal-analysis curves ceased to appear on the fluoranthene side when the concentration of this hydrocarbon was 70 wt.%, and on the phenanthrene side when the phenanthrene concentration was 65 wt.%. From this it is possible to conclude that large regions of limited solid solutions are present in the system on the sides of both components. In all of the experiments the delay in crystallization did not exceed 2° when the molten mixtures were cooled with vigorous stirring.

7. System fluoranthene-fluorene. It should be mentioned that in this system the curves of the start of crystallization show an extremely symmetrical arrangement. The coordinates of the eutectic point are: equilibrium-phase temperature 69.0° and fluoranthene concentration 56.74 wt.% (51.9 mole %). The fluoranthene crystallized from the molten mixtures with a supercooling of 1-3°, while for fluorene it was 2-4°.
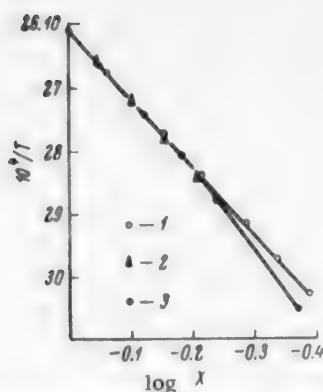
Fig. 2. Solubility of fluoranthene in naphthalene (1), phenanthrene (2), and durene (3).
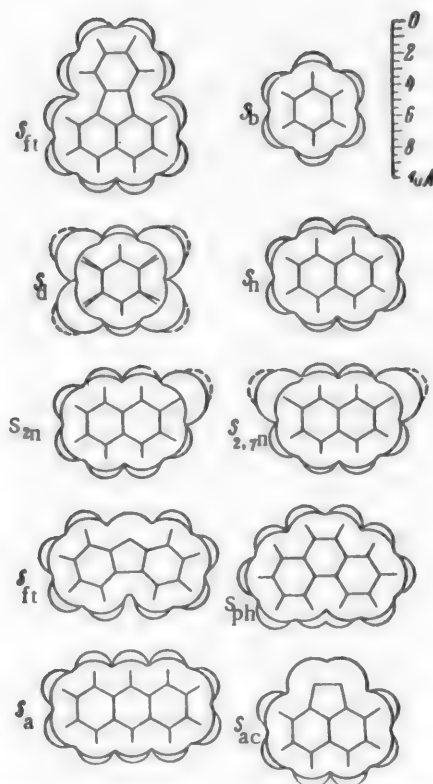
Fig. 3. Cross sections of molecular models: S_{ft} — fluoranthene, S_b — benzene, S_d — durene, S_n — naphthalene, S_{2n} — 2-methylnaphthalene, $S_{2,7n}$ — 2,7-dimethylnaphthalene, s_{fl} — fluorene, S_{ph} — phenanthrene, S_a — anthracene, S_{ac} — acenaphthene.

8. System fluoranthene-anthracene. The eutectic was characterized by a temperature of 101° and a fluoranthene content of 88.40 wt. % (87.0 mole %). Second eutectic rests were observed in all of the investigated mixtures except one. This excludes the presence of a large region of solid solutions of fluoranthene in anthracene. Fluoranthene, crystallizing from the melt together with anthracene, apparently forms limited solid solutions of low concentration with the latter. A large difference in the melting points of the system components (100°) was responsible for the unsymmetrical appearance of the phase diagram. The degree of supercooling, required for the appearance of the first crystals of anthracene and fluoranthene from the vigorously stirred molten mixtures, was 2-4°.

9. System fluoranthene-acenaphthene. Here the eutectic crystallizes at 61.8°, and the fluoranthene concentration in the mixture is 50.58 wt. % (43.8 mole %). In cooling the melts, eutectic rests were observed on the temperature-time curves of all of the mixtures (with one exception). Both components crystallized from the melts almost without supercooling, and the latter did not exceed 0.5-1°.

Calculation of the Fusion Heat of Fluoranthene

Very little experimental data exists in the literature on the latent heats of fusion of aromatic hydrocarbons. Thus we do not have any information on calorimetric studies of the heat of fusion of fluoranthene. The obtained thermal analysis data can be used to calculate this value.

We will assume that the studied eutectic systems obey the equation derived by I. F. Shreder [5] for ideal solutions: $\ln X = Q(1/T - 1/T_1)/R$, where X is the mole fraction of fluoranthene, R is the gas constant, equal to 1.985 cal/mole, T is the melting point, T_1 is the initial crystallization temperature of fluoranthene, and Q is the sought heat of fusion. If approximately the same values of Q are obtained when the experimentally found values of X and T_1 are substituted in the Shreder equation, then this supports the assumption made that the corresponding binary system approaches the ideal type.

The performed calculations revealed that relatively constant values of Q are obtained for fluoranthene when based on the thermal-analysis data for the system fluoranthene-naphthalene. The average value of the heat of fusion (crystallization) for fluoranthene is approximately equal to 4300 cal/mole. Similar calculations of the Q for fluoranthene, based on the found values of X and T_1 for the systems fluoranthene-fluorene and fluoranthene-2-methylnaphtalene, showed a somewhat lesser constancy of the Q values than for the system fluoranthene-naphthalene.

The above is clearly illustrated by plotting the solubility of fluoranthene in naphthalene, fluorene and 2-methylnaphtalene in the coordinates log X and $10^4/T$ (Fig. 2): the points for the system fluoranthene-naphthalene fall closer to a straight line than do the points for the other systems.

Molecular Structure and Type of Phase Diagram

We will discuss the molecular structure and dimensions of the components of the investigated systems, and we will compare this structure data with the type of phase diagram. We will utilize existing data on the x-ray and electronographic determination of the fine structure of aromatic hydrocarbon molecules. Structure characteristics of this type were obtained for benzene, durene, naphthalene, fluorene, anthracene and acenaphthene. The centers of the carbon atoms in the molecules of these compounds are found approximately in one plane. The existing data [6] on interatomic distances and valence angles indicate a slight difference in the dimensions of structurally similar elements in the molecules of the mentioned hydrocarbons, which permits utilizing the following average values of the valence bonds and angles in constructing the molecular models:

$$C\!-\!C_{ar} = 1.4 \text{ Å}, \ C\!-\!C_{al.} = 1.5 \text{ Å}, \ C_{ar.}\!-\!H = 1.0 \text{Å}, <C\!-\!C\!=\!C_{at} = 120°.$$

Using this data we constructed the internal cross-section contours of the schematic molecular models of all of the components(excepting acenaphthene)of the systems studied in the present paper (Fig. 3). For acenaphthene the distance $CH_2 - CH_2$ was taken equal to 1.62 A [7]. To construct the external cross-section contours of all of the models shown in Fig. 4 we used the intermolecular radii of approach [8]: R_C = 1.72 A and R_H = 1.17 A.

In the case of durene and the naphthalene homologs, the hydrogen atoms of the methyl groups linked to the aromatic ring fall only partially in the cross-section plane of the molecular model. Consequently they are shown conditionally in the cross section of each methyl group as a crescent-shaped cross section of only one H atom. A deviation of $\approx 3°$ in the angle of adjacent repulsing methyls is shown in the cross section of the durene model.

We also determined the cross-section areas of the molecular models shown in Fig. 3. They proved to be approximately (+1 A^2) as follows: S_{ft} of fluoranthene $\approx$ 72 A^2, S_b of benzene $\approx$ 33 A^2, S_d of durene $\approx$ 53 A^2, S_n of naphthalene $\approx$ 49 A^2, S_{2n} of 2-methylnaphthalene $\approx$ 54 A^2, $S_{2,m}$ of 2,7-dimethylnaphthalene $\approx$ 59 A^2, S_{ph} of phenanthrene $\approx$ 66 A^2, S_{fl} of fluorene $\approx$ 60 A^2, S_a of anthracene $\approx$ 65 A^2, and S_{ac} of acenaphthene $\approx$ $\approx$ 56 A^2.

Consequently, the cross-section area of the molecular model of fluoranthene is larger than the cross-section areas of the molecular models of any of the nine components of the studied systems.

On the whole, the eutectic nature of the nine fluoranthene-containing systems described above, revealed as a result of the performed experiments, fits in well with the variation in the shapes and sizes of the component molecules. In eight of the nine combinations the ratio of the cross-section areas of the molecular models of the components exceeds 10-15%. According to our earlier established rule [10] this fully explains the eutectic type of phase diagrams, even in the case of systems formed from components having a similar molecular shape. Here, together with the indicated large deviation in the size of the areas, we also have a large variation in the cross-section shapes of the molecular models of the components of the systems.

Indications of the formation of limited solid solutions were revealed only for the eutectic system fluoranthene-phenanthrene. It is characteristic that it is specifically this pair of compounds that differ less than the other, both in the cross-section shapes of their molecular models (this appears when the model cross-sections are superimposed) and in their size.

Fluoranthene crystals have the following ratios of the axis and lattice parameters [9]: a : b : c = 2.975 : :1:3.563; a = 18.46, b = 6.205, c = 22.11; $\angle \beta$ 121° 45', n = 8, F.c. $P2_1$ /C. Two fluoranthene molecules form one asymmetric unit in the elementary cell of the crystal. The similar values (a, b, c, β) for the second components of the investigated systems differ substantially from the parameters given for fluoranthene. This difference can also be explained by assuming that continuous solid solutions are absent in the investigated systems.

DISCUSSION OF RESULTS

In the present paper, nine binary systems, containing fluoranthene and a second component of variable shape and structure, were discussed (Fig. 3). The second components were: benzene and one of its homologs, naphthalene and two of its homologs, and also the prototypes of four important homologous series of trinuclear aromatic hydrocarbons, namely phenanthrene, anthracene, fluorene and acenaphthene.

Based on the fact that the systems of fluoranthene with benzene and with durene were found to be of the eutectic type, and taking into account the molecular-structure comparisons made in the previous section, it becomes possible to predict that all systems containing fluoranthene and a benzene hydrocarbon (toluene, xylenes, ethylbenzene, trimethylbenzene, etc.) will have a similar eutectic type of phase diagram, since substantial structural differences in the molecules of the components will appear in all of these combinations. The fact that the same type of system was shown for the case of fluoranthene with naphthalene, 2-methylnaphthalene and 2,7-dimethylnaphthalene serves as a basis to prognosticate that all systems containing fluoranthene and a hydro-carbon of the naphthalene series, the latter also being structurally quite different from fluoranthene,. will have an eutectic type of phase equilibrium. The fact that an eutectic type of system was found to exist for the case of fluoranthene with phenanthrene, anthracene, fluorene and acenaphthene gives basis to predict that the same type of system will also hold for the case of fluoranthene with the homologs (mono-, di- and polymethyl, ethyl, etc) of these trinuclear aromatic hydrocarbons. Here also, as a rule, a large difference in the structure of the components will be manifested. In practice, the postulated combinations, representing uninvestigated systems containing fluoranthene, are found in the industrial products (tars, oils) obtained from the processing of fuel resources (petroleum, coal, etc.).

SUMMARY

1. Nine two-component systems were studied, composed of fluoranthene in combination with some of the mono-, bi- and trinuclear hydrocarbons associated with it in the technical mixtures obtained from the hydrolysis of fuel resources. The studied systems were found to be of the eutectic type.

2. The calculated fusion heat of fluoranthene was found to be approximately 4300 cal/mole. The type of phase diagram found was explained by taking into consideration the shapes and dimensions of the cross sections of the molecular models of the system components. The type of a number of unstudied systems containing fluoranthene was predicted.

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REACTION BETWEEN SODIUM TUNGSTATE AND 4,4'-BIS (3,4-DIHYDROXYPHENYLAZO)-2,2'-STILBENEDISULFONIC ACID ("STILBAZO") IN AQUEOUS SOLUTIONS

II. ACTION OF ORGANIC SOLVENTS AND EFFECT OF SOME SALTS

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In the previous paper [1] we had shown that with excess stilbazo the optical density of acid mixtures of sodium tungstate and stilbazo is composed of the light absorption of the stilbazo-tungstate compound and the blue suspension of excess reagent. For this reason the relationship between the optical density and the tungstate concentration is not a straight-line function.

In this paper we investigated the action of some organic solvents for the purpose of separating stilbazo and the stilbazo-tungstate compound. In addition, we investigated the effect of certain salts on the reaction between the tungstate and stilbazo in solution.

The stilbazo reagent was purified as described earlier [1].

ACTION OF ORGANIC SOLVENTS

To effect a separation of the stilbazo-tungstate compound from excess stilbazo we investigated the action of the following groups of organic solvents: 1) chloroform, carbon tetrachloride, dichloroethane, benzene, toluene and ethyl bromide; 2) butyl alcohol, isobutyl alcohol and ethyl acetate; and 3) acetone, methyl alcohol and ethyl alcohol.

Aqueous solutions of stilbazo and a solution of the stilbazo-tungstate compound, without an excess and with an excess of one of the components, were shaken in a separatory funnel with one of the mentioned solvents.

In acid solutions the solvents of the first group cause both the blue stilbazo suspension and the stilbazo-tungstate compound to float at the interface. The other solvents prove to be excellent solvents for the blue stilbazo suspension with the formation of either yellow or orange solutions, in the aqueous phase if the organic solvent is water soluble, and in the nonaqueous phase if the organic solvent is insoluble in water. Here the stilbazo-tungstate compound also shows more or less partial decomposition. Of the solvents in this group, in strongly acid solutions, only methanol can barely dissolve the precipitate or decompose the solution of stilbazo-tungstate compound.

Use can be made of the described action of organic solvents to dissolve the stilbazo suspension and effect a separation of stilbazo-tungstate compound from excess stilbazo. The action of methanol and benzene was studied in greater detail.

The optical density of the solutions was measured using a FM universal photometer of the Pulfrich type and a M 57 light filter (effective wavelength 574 mμ).

The relationship between the optical density of stilbazo solutions and the concentration at pH 1, with and without the addition of methanol, is shown in Fig. 1. The total volume of each solution was 50 ml. In the case of the methanol-containing mixtures each such volume contained 7 ml of an acid methanol solution (ratio of methanol to 0.2N hydrochloric acid = 1:1).
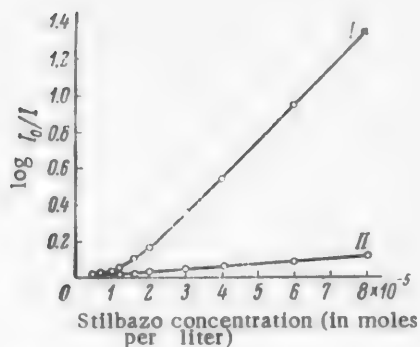
Fig. 1. Relationship between the optical density of stilbazo solutions and the concentration.

1) without adding methanol (blue solutions), II) mixtures containing methanol (yellow solutions), pH 1. Cuvette 10 mm.

Fig. 2. Relationship between the optical density and the mole ratio stilbazo /tungstate. I) without methanol, II) with methanol added, III) with correction for the actual optical density of excess stilbazo. $Na_2WO_4 = 3.3 \cdot 10^{-4}$ mole/liter. pH 1. Cuvette 10 mm.

From Fig. 1 it can be seen that the optical density of aqueous acid solutions of stilbazo shows much greater change with increase in the stilbazo concentration than does the optical density of aqueous alcohol solutions. This is due to the formation of a blue suspension of stilbazo in the aqueous acid solutions. In aqueous alcohol solutions the blue suspension either does not form or it dissolves when methanol is added to give either yellow or orange solutions.

The relationship between the optical density of mixtures composed of stilbazo and sodium tungstate solutions (pH 1)and the molar ratio [stilbazo]:[Na_2WO_4] at a constant tungstate concentration, with or without the addition of methanol, is shown in Fig. 2. Here the volume of each solution was 60 ml. In this case the aqueous alcohol solutions contained 15 ml of a mixture of methanol and 1N hydrochloric acid (methanol: acid = 9:1) in each volume. The alcohol mixture was added 2 hours after the components had been mixed with hydrochloric acid [1] and about 5-10 minutes before measuring the optical density.

Curves I and II in Fig. 2 coincide provided the solutions contain an excess of tungstate. * A decomposition of the stilbazo-tungstate compound by methanol is not observed under these conditions. With excess stilbazo the optical density of the aqueous alcohol solutions is considerably less than in the absence of the alcohol, since methanol dissolves the blue suspension of excess stilbazo, converting it to a yellow solution: curve II approaches curve III, plotted from the data in which the effect of the actual optical density of the free stilbazo (excess) on the total density of the solutions had been eliminated. For this reason, with a constant concentration of excess stilbazo, changes in the optical density of aqueous alcohol solutions as a function of a variable tungstate concentration are expressed by lines that approach a straight line. At low tungstate concentrations,reaction between stilbazo and tungstate is completely masked by the blue color of the stilbazo suspension. A formation of the stilbazo-tungstate compound under these conditions can be shown only after methanol is added to the solution. It is possible to detect 5-10 micrograms of tungsten in 10-15 ml of the final aqueous alcohol solution.

The slight solubility of the stilbazo-tungstate compound under the described conditions can be shown by shaking the acid (0.1N HCl) aqueous alcohol mixture with a precipitate of the stilbazo-tungstate compound. The solution assumes a light-yellow color after the precipitate has settled. The solubility is reduced even further when the acidity is increased. When the acid concentration is 0.5 to 1N the aqueous alcohol mixture over the precipitate remains

*Stilbazo and sodium tungstate react in a 1:2 ratio when the acidity of the solution is 0.1N or greater [1].

colorless. At such a high acidity both the coagulation of stilbazo in aqueous solution and of the stilbazo-tungstate compound in aqueous and aqueous alcohol solutions are accelerated. This circumstance can be used to separate the stilbazo-tungstate compound from excess stilbazo.

Three mixtures were prepared, each containing $1.3 \cdot 10^{-4}$ mole/liter of stilbazo and varying amounts of sodium tungstate and 0.33N acid. In all of the solutions the stilbazo was present in excess over the tungstate. One hour after mixing, each solution was treated with $^1/_3$ its volume of methanol. After mixing, the solutions were separated from the precipitate by filtering through No. 3 glass filters. The filtrates were yellow. The precipitates were washed with aqueous acid-alcohol mixture(1 part of alcohol to 3 parts of 0.33N acid) until the effluent wash liquor was clear. The washed precipitates were dissolved in equal volumes of pure methanol. The solutions had a yellow color. The optical density of these solutions, measured using a M 43 light filter (effective wavelength 436 mμ), was compared with the concentration of tungstate in the corresponding aqueous solutions, from which the stilbazo-tungstate compound had been removed by precipitation:

Optical density of alcohol
    solutions ($\log I_0/I$). . . . . 0.34,   0.67,   1.35.
Concentrations of tungstate in original
    solutions (in moles/liter) . . . . $0.4 \cdot 10^{-4}$, $0.8 \cdot 10^{-4}$, $1.6 \cdot 10^{-4}$.

A direct proportionality between the tungstate concentration in the original solutions and the optical density values of the alcohol solutions of the precipitates is evidence that a good separation of stilbazo-tungstate compound from excess stilbazo had been achieved.

Reaction between stilbazo and tungstate is strongly hindered by methanol. For this reason the alcohol or its acid mixture should be added to the solution after reaction between stilbazo and the tungstate has ended, i.e. 2 hours after the reactant mixture has been acidified [1].

JOINT ACTION OF METHANOL AND BENZENE

Above, it had been indicated that both stilbazo and the stilbazo-tungstate compound float at the interface when the acid aqueous solutions are shaken with benzene or the other solvents of the first group. Here the blue aqueous solutions become colorless, while the benzene layer above the interface remains colorless. The higher the acidity of the aqueous solution, the more effective the flotation.

The flotation of the stilbazo-tungstate compound is equally effective whether from aqueous alcohol solutions or in the absence of alcohol, whereas benzene fails to cause the flotation of stilbazo from aqueous alcohol solutions no matter what the acid content. The flotated stilbazo-tungstate compound is easily decomposed with either caustic solution or ammonia. Here the solution assumes either an intense violet or blue color, characteristic for alkaline stilbazo solutions.

Making use of these properties, the stilbazo-tungstate compound can be separated from excess stilbazo. By dissolving the precipitate of stilbazo-tungstate compound in alkali solution and measuring the optical density of the alkaline solution, it becomes possible to determine the amount of tungstate in the original solution.

A mixture of tungstate and stilbazo solutions in a separatory funnel is treated with sufficient 0.5-1N hydrochloric acid to give a 0.1N solution of the latter in the final volume. After 2 hours, sufficient acid is added to bring the concentration up to 0.2-0.3N, and also benzene in an amount approximately equal to approximately half the volume of the aqueous solution. The mixture is shaken well until the aqueous phase has become clear. Then sufficient hydrochloric acid-methanol mixture (2 ml of concentrated acid per 100 ml of alcohol) is added to dissolve all of the stilbazo precipitate. The required amount of alcohol is determined in a previous experiment omitting the tungstate. The shaking is continued for 1-2 minutes. After stratification the yellow aqueous alcohol solution of stilbazo is separated from the nonaqueous phase and flotated stilbazo-tungstate compound. The aqueous alcohol solution entraps a small amount of the flotated stilbazo-tungstate compound, for which reason it is suction-filtered through a No. 3 glass filter. The benzene phase with flotated stilbazo-tungstate compound and the precipitate on the filter are washed several times with acidulated aqueous alcohol mixture (1 volume of alcohol to 3 volumes of 0.4N hydrochloric acid). The flotated stilbazo-tungstate compound and the precipitate on the filter are dissolved in a known volume of a 1% hydroxylamine hydrochloride solution in

1N soldium hydroxide solution. •   A M 57 light filter is used to measure the optical density.

When a solution containing only stilbazo (in the absence of tungstate) is treated in this manner a hardly visible film remains at the interface, apparently being a small amount of the flotation agent in stilbazo. This film dissolves in caustic solution with a faint violet color. In determining the amount of tungstate the intensity of this color should be substracted, as a "blank" experiment correction.

Using this method, we processed solutions that contained various concentrations of tungstate and constant concentrations of stilbazo ($1 \cdot 10^{-4}$ mole/liter). The volume of each mixture after adding enough hydrochloric acid to make it 0.1N in HCl was 20 ml.   The volume of the final alkaline solution was 50 ml in every case. The relationship between the optical density of the alkaline solutions and the tungstate concentration in the original solutions is shown in Fig. 3.   The values given for $\log I_0/I$ include the "blank" experiment correction, which under the described conditions is 0.06.
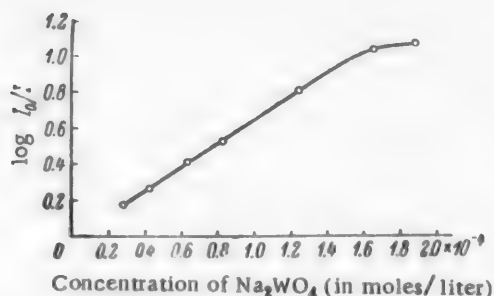
Fig. 3. Relationship between the optical density of alkaline solutions after methanol-benzene treatment and the concentration of tungstate in the original solutions.
Cuvette 10 mm.
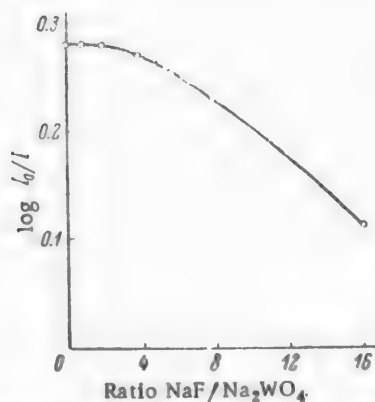
Fig. 4. Relationship between the optical density and the mole ratio NaF/Na$_2$ WO$_4$. [Na$_2$WO$_4$] = $1.25 \cdot 10^{-4}$ mole/liter,[stilbazo] = $0.75 \cdot 10^{-4}$ mole/liter,pH 1. Cuvette 10 mm

From Fig. 3 it can be seen that the change in the optical density of the alkaline solutions is proportional to the amount of tungstate in the original solutions.   The last two points do not fall on a straight line because of an insufficient excess of stilbazo to tie up all of the tungstate in the corresponding original solutions.

The discussed action of organic solvents serves as evidence that aqueous solutions of the stilbazo-tungstate compound possess a colloidal character.

EFFECT OF VARIOUS COMPOUNDS

Phosphoric acid. Phosphate ions even in low concentration prevent reaction between sodium tungstate and stilbazo. Absolutely no stilbazo-tungstate compound is formed even with a 4-fold excess of phosphoric acid on the tungstate concentration ($1.25 \cdot 10^{-10}$ mole/liter). With equivalent concentrations of sodium tungstate and phosphoric acid ,the optical density of the solutions is approximately 25% less than in the absence of phosphoric acid.

Sodium fluoride. The effect of adding sodium fluoride on the optical density of solutions containing tungstate, stilbazo and 0.1 N hydrochloric acid is shown in Fig. 4. The hindering action of sodium fluoride on reaction between tungstate and stilbazo becomes noticeable when the sodium fluoride concentration is several times that of the tungstate.

Sodium chloride, sulfate and nitrate and ammonium chloride. At concentrations not exceeding 0.01-0.02 N , the indicated salts fail to either hinder reaction between tungstate and stilbazo or affect the optical density. Concentrations of 0.1N and higher lead to the formation of precipitates that are colored either blue or violet or even brown (in the case of NaNO$_3$). The effect of sodium chloride was studied in more detail. Here a precipitate appears even at a pH of 2 to 3, whereas in the absence of the salt the blue-stilbazo-tungstate compound is either

• The optical density of alkaline stilbazo solutions drops rapidly.   The optical density remains constant for at least a day if hydroxylamine hydrochloride is added.

not formed or is formed with difficulty. Sodium chloride accelerates reaction between tungstate and stilbazo; the stilbazo-tungstate compound is completely coagulated within $\frac{1}{2}$ -1 hour after mixing the reactants. The solution above the precipitate becomes colorless due to the coprecipitation of excess stilbazo with the stilbazo-tungstate compound. Treatment with methanol and benzene, as described above, revealed that even with a 1N concentration of NaCl the stilbazo-tungstate compound separates completely from the excess stilbazo, and the optical density of the final alkaline solutions is directly proportional to the tungstate concentration in the original solutions.

Sodium molybdate. Stilbazo reacts with sodium molybdate in a broader acid range than it does with sodium tungstate; here either colored solutions or precipitates are formed. Consequently, sodium molybdate masks the reaction between stilbazo and tungstate. However, if the molybdate concentration does not exceed the tungstate concentration, the masking action of the molybdate can be eliminated by the methanol-benzene treatment. Under these conditions the optical density of the final alkaline solutions is the same as in the absence of molybdate.

Stannous and stannic chlorides. The tin chlorides react with stilbazo in weakly acid and acid solutions. The mixing of stilbazo solutions with more concentrated acid solutions of stannous chloride yields blue precipitates, which then in a matter of several minutes go into solution. The blue color of the resulting solutions gradually changes to a pink, and then the solutions become colorless.

The precipitates obtained when solutions of stilbazo and stannic chloride are mixed go into solution when methanol is added. The solutions assume a transitory lilac (pink with a violet tinge) color. When mixed solutions of stilbazo, tungstate and either stannic or stannous salt of variable component concentration are given the methanol-benzene treatment, the optical density of the final alkaline solutions is noticeably less than in the absence of tin salt. Consequently, tin salts hinder reaction between stilbazo and tungstate.

Nickel chloride. Nickel chloride does not react with stilbazo in neutral and acid solutions. The color communicated to an acid solution by the nickel salt at a concentration of 10^{-3}- 10^{-4} mole/liter is insignificant when compared with the color intensity of a solution of the stilbazo-tungstate compound at a tungstate concentration of the order of 10^{-4} mole/liter. The optical density of the final alkaline solutions after a methanol-benzene treatment of acid solutions, containing stilbazo, tungstate and a 200-fold excess of nickel chloride, is the same as in the absence of the nickel salt, while with a 500-fold excess it is less by approximately 20%.

Boric acid, sodium tetraborate and sodium fluoborate. Precipitates of the stilbazo-tungstate compound deposit from 0.1M sodium fluoborate solutions and from saturated sodium tetraborate or boric acid solutions. The optical density of the final alkaline solutions after the methanol-benzene treatment is the same as in the absence of these compounds. However, the addition of either boric acid or sodium tetraborate to solutions containing, besides stilbazo and tungstate, also sodium fluoride, does not completely eliminate the masking effect of the latter.

SUMMARY

1. The action of some organic solvents on the solutions and precipitates of both stilbazo and the blue stilbazo-tungstate compound was investigated.

2. It was shown that using methanol or methanol together with benzene makes it possible to separate the stilbazo-tungstate compound from excess stilbazo in acid solutions.

3. Phosphoric acid, sodium fluoride, sodium molybdate and tin salts interfere in the reaction between sodium tungstate and stilbazo; nickel chloride, boric acid, sodium tetraborate and sodium fluoborate do not interfere.

Alkali metal salts at concentrations above 0.01-0.02 N accelerate both reaction between sodium tungstate and stilbazo and coagulation of the stilbazo-tungstate compound.

4. The use of methanol alone or of methanol together with benzene makes it possible to determine up to 5-10 micrograms of tungsten in 10-15 ml of solution. In this connection neither sodium molybdate in concentrations below the tungstate concentration nor high concentrations of alkali metal salts interfere.

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REACTION OF CYCLOPROPANE HYDROCARBONS WITH MERCURIC SALTS

IX. γ-MERCURATED ALCOHOLS AND THEIR ETHERS FROM ARYLCYCLOPROPANES

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The opening of the three-membered ring in phenylcyclopropane using mercuric acetate was described in one of our earlier communications [1]. In this paper we studied the action of mercuric acetate in aqueous and methanol solutions on arylcyclopropanes containing either a methyl or a methoxy group in the para-position of the benzene ring.

It was established that reaction here proceeds under the same conditions as in the case of phenylcyclopropane, i.e. by shaking the reaction mixture in the cold for many hours. The addition of mercuric acetate in either aqueous or methanol solution to the two arylcyclopropanes (p-anisyl and p-tolylcyclopropane) leads to the respective formation of 3-hydroxy-3-arylpropylmercuric acetates and 3-methoxy-3-arylpropylmercuric acetates; when reacted with various potassium salts these mercuric acetates were converted to the corresponding crystalline salts of γ-mercurated alcohols and their methyl ethers.

(Ia) and (IIa): $Ar = p\text{-}CH_3OC_6H_4$; (Ib) and (IIb) $Ar = p\text{-}CH_3C_6H_4$; $X = Cl$, Br, I, CN, CNS.

The preparation of crystalline organomercury compounds (not described in the literature) may serve as a way of identifying both p-anisyl- and p-tolylcyclopropane.

Using one of them as an example (3-hydroxy-3-p-anisylpropylmercuric acetate), the structure of the obtained γ-mercurated secondary alcohols was established by our earlier developed method [2], namely, by heating with zinc dust. This reaction, including the intermediate symmetrization stage and the subsequent thermal decomposition of the symmetrization products, leads to the formation of a secondary alcohol and a ketone, both having the carbon skeleton of the original organomercury compound.

40

The thus-obtained alcohol and ketone were identified by preparing crystalline derivatives, the 3,5-dinitro-benzoate in the case of the alcohol and the 2,4-dinitrophenylhydrazone in the case of the ketone.

EXPERIMENTAL

γ-Mercurated alcohols and their methyl ethers from p-anisylcyclopropane. p-Anisylcyclopropane (25 g, b.p. 223.5-224° for 745 mm, n_D^{20} 1.5329, d_4^{20} 1.0011, MR_D 45.95. $C_{10}H_{12}O_F{}_3\triangle$. Calculated 44.92, EM_D 1.03; obtained by the decomposition of 3-p-anisylpyrazoline [3] was shaken with a solution of 54 g of mercuric acetate in 400 ml of distilled water for 24 hours at room temperature. The end of reaction was determined by the disappearance of the upper layer. The obtained heavy oil was separated, and then combined with the ether extracts of the water layer; the ether, water and acetic acid were vacuum distilled, while the residue was again dissolved in ether and the solution filtered. After several hours white crystals of 3-hydroxy-3-p-anisyl-propyl-mercuric acetate (Ia) deposited from the filtrate.

The reaction of mercuric acetate (13 g) with p-anisylcyclopropane (6 g) in methanol solution (200 ml of anhydrous methyl alcohol) was run under the same conditions. At reaction end (absence of mercuric salt in the solution, determined by testing with alkali) the methyl alcohol and acetic acid were vacuum distilled; the yield of 3-methoxy -3-p-anisylpropylmercuric acetate (IIa; oil) was 10 g (55 %).

TABLE 1

Crystalline Organomercury Compounds of Structure p-CH₃OC₆H₄CHCH₂CH₂HgX

OR

OR	X	Name	Melting point	Yield (in %)	Hg (%) found	Hg (%) calculated
OH	OCOCH₃	3-Hydroxy-3-p-anisylpropyl-mercuric acetate	112—113°	45	47.63, 47.41	47.41
OH	Cl	3-Hydroxy-3-anisylpropyl-mercuric chloride	75—76	82	49.57, 49.65	49.99
OH	Br	3-Hydroxy-3-p-anisylpropyl-mercuric bromide •	83—84	90	45.61, 45.12	45.01
OH	I	3-Hydroxy-3-p-anisylpropyl-mercuric iodide	70.5—71	85	40.33, 40.54	40.70
OCH₃	Cl	3-Methoxy-3-p-anisylpropyl-mercuric chloride ••	74—75	74	48.20, 48.44	48.31
OCH₃	Br	3-Methoxy-3-p-anisylpropyl-mercuric bromide •••	71—71.5	92	44.11, 43.80	43.62
OCH₃	I	3-Methoxy-3-p-anisylpropyl-mercuric iodide	87—87.5	72	—	—
OCH₃	CN	3-Methoxy-3-p-anisylpropyl-mercuric cyanide	78.5—79	86	49.51, 49.73	49.41
OCH₃	CNS	3-Methoxy-3-p-anisylpropyl-mercuric thiocyanate	93.5—94	89	45.52, 46.15	45.81

•Found %: C 26.84, 26.73; H 3.20, 3.00. $C_{10}H_{13}O_2BrHg$. Calculated %: C 26.94; H 2.94.

• •Found %: C 31.66, 31.75; H 3.59; 3.57. $C_{11}H_{15}O_2ClHg$. Calculated %: C 31.74; H 3.87.

• ••Found %: C 28.50, 28.90; H 3.38, 3.37. $C_{11}H_{15}O_2BrHg$. Calculated %: C 28.73; H 3.29.

The mercuric acetates (Ia) and (IIa) were converted in conventional manner (reaction with postassium salts in aqueous solution) to the mercuric halides, mercuric cyanides and mercuric thiocyanates. The melting points (after recrystallization from petroleum ether), yields and analysis data for the crystalline γ-mercurated alcohols obtained from p-anisylcyclopropane, as well as for their methyl ethers, are given in Table 1.

When the first member in the series of obtained γ-mercurated alcohols, namely 3-hydroxy-3-p-anisyl-propylmercuric acetate (50 g), was warmed with zinc dust (16 g), a vigorous reaction set in and the thermal decomposition products began to distil. After reaction was over the distillate was separated from a small amount of mercury and redistilled. The fraction with b.p. 106-128° (5 mm) was collected, being a mixture of ethyl-p-anisylcarbinol (b.p. 138° for 22 mm; 251° for 760 mm [4]) and ethyl p-anisyl ketone (b.p. 145-147° for 14 mm [5]; 136-139° for 12 mm [6]); yield 18 g (~ 90%). That these two reaction products were present in the 105-128° fraction was established by preparing the 3,5-dinitrobenzoate of ethyl-p-anisylcarbinol from one portion, and the 2,4-dinitrophenylhydrazone of ethyl p-anisyl ketone from a second portion. Since the 3,5-dinitrobenzoate derivative was obtained as an oil, it was converted to the α-naphthylamine derivative (new in the literature) with m.p. 102-103° (after recrystallization from ethyl alcohol).

Found %: N 8.05, 8.27. $C_{27}H_{25}O_7N_3$. Calculated %: N 8.15.

The mixed melting point with the α-naphthylamine derivative of the 3,5-dinitrobenzoate obtained from authentic ethyl-p-anisylcarbinol was not depressed.

The 2,4-dinitrophenylhydrazone had m.p. 188-189° (new in the literature).

Found %: N 16.70, 16.82. $C_{16}H_{16}O_5N_4$. Calculated %: N 16.28.

The mixed melting point with the 2,4-dinitrophenylhydrazone of authentic ethyl p-anisyl ketone was not depressed.

γ-Mercurated alcohols and their methyl ethers from p-tolylcyclopropane. p-Tolylcyclopropane (6 g, b.p. 194-194.5° for 745 mm, n_D^{20} 1.5241, d_4^{20} 0.9227, MR_D 43.82. $C_{10}H_{12}$ F₃△. Calculated 43.29, EM_D 0.57; obtained by the decomposition of 3-p-tolylpyrazoline [3]) was shaken with aqueous mercuric acetate solution (14.5 g in 150 ml of distilled water) for 12 hours at room temperature. The reaction in methanol solution (200 ml of anhydrous methyl alcohol) was run with the same amounts of reactants and under the same conditions. The isolation of the reaction products, 3-hydroxy-3-p-tolylpropylmercuric acetate (Ib) and 3-methoxy-3-p-tolyl-propylmercuric acetate (IIb) — and their conversion to the corresponding mercuric halides, mercuric cyanides and mercuric thiocyanates were accomplished as described above.

The organomercury compounds obtained from p-tolylcyclopropane proved for the most part to be noncrystallizing oils; the melting points of the crystalline salts (after recrystallization from petroleum ether), and their yields and analysis data are given in Table 2.

TABLE 2

Crystalline Organomercury Compounds of Structure p-$CH_3C_6H_4CH$ — CH_2CH_2HgX

OR

OR	X	Name	Melting point	Yield (in %)	Hg (%) found	Hg (%) calculated
OH	OCOCH₃	3-Hydroxy-3-p-tolylpropyl-mercuric acetate	68—69°	54	49.62, 49.49	49.06
OCH₃	Cl	3-Methoxy-3-p-tolylpropyl-mercuric chloride	71—72	84	50.34, 50.25	50.23
OCH₃	Br	3-Methoxy-3-p-tolylpropyl-mercuric bromide	73—74	73	45.95, 45.32	45.20

SUMMARY

1. The reaction of mercuric acetate in either aqueous or methanol solution with p-anisylcyclopropane and p-tolylcyclopropane results in the cleavage of the three-membered ring and the formation of γ-mercurated alcohols and their methyl ethers, and specifically, of 3-hydroxy- and 3-methoxy-3-arylpropylmercuric acetates,

which when reacted with the proper potassium salts are converted to the corresponding mercuric halides, mercuric cyanides and mercuric thiocyanates.

2. The structure of the obtained organomercury compounds was established on the basis of 3-hydroxy-3-p-anisylpropylmercuric acetate, which when heated with zinc dust was converted to ethyl-p-anisylcarbinol and ethyl p-anisyl ketone.

3. The preparation of crystalline organomercury compounds can serve as a means of identifying p-anisyl-cyclopropane and p-tolylcyclopropane.

4. The following crystalline organomercury compounds are new: 3-hydroxy-3-p-anisylpropylmercuric acetate and the corresponding chloride, bromide and iodide; 3-methoxy-3-p-anisylpropylmercuric chloride and the corresponding bromide, iodide, cyanide and thiocyanate; 3-hydroxy-3-p-tolylpropylmercuric acetate; 3-methoxy-3-p-tolylpropylmercuric chloride and the corresponding bromide.

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*Original Russian pagination. See C. B. translation.

CYCLOPROPANES AND CYCLOBUTANES

V. ARYLCYCLOPROPANES IN ALKYLATION

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Some physical and chemical properties of phenyl-, p-tolyl- and p-anisylcyclopropane were described in our earlier communications. It was shown that the three-membered ring in these arylcyclopropanes is easily cleaved when the cyclopropane is treated with mercuric acetate in either aqueous or alcohol solution [1,2]; this reaction emphasizes the similarity in the chemical behavior of styrene derivatives [3, 4] and arylcyclopropanes.

A similarity of the three-membered ring in arylcyclopropanes to the double bond in the corresponding styrene derivatives also appears in its ability to conjugate with the the aromatic ring, which was observed even by N. M. Kishner [5] (based on the high molecular-refraction exaltation shown by 1,2-diphenylcyclopropane), and which was established by us [6] in studying the Raman spectrum of phenylcyclopropane (based on a large increase in the intensities of the characteristic frequencies in the spectrum, since such an increase is usually peculiar to hydrocarbons with a conjugated system of double bonds). A study of the UV-absorption spectra [6] of phenyl-p-tolyl- and p-anisylcyclopropane enabled us to first establish that conjugation between the three-membered ring and the aromatic nucleus increases when either a methyl group or a methoxyl group is introduced into the aromatic nucleus; the validity of such a rule was also indicated by the increase in the molecular refraction exaltation when going from phenylcyclopropane to p-tolyl- or p-anisylcyclopropane.

In this paper we studied the behavior of phenylcyclopropane in the alkylation of benzene, toluene and anisole, and also that of p-tolyl- and p-anisylcyclopropane in the alkylation of benzene. From the literature on the alkylation of aromatic hydrocarbons with alkylcyclopropanes [7-12] it follows that aluminum chloride does not cause a previous isomerization of cyclopropanes to alkenes [8, 12]; consequently, this catalyst was used in the present study.

The alkylation of benzene with phenylcyclopropane* gave a 52 % yield of 1,1-diphenylpropane.

$$C_6H_5H + \underset{\underset{CH_2}{\diagdown}}{\overset{\overset{C_6H_5}{|}}{CH}}-CH_2 \xrightarrow{AlCl_3} C_6H_5-\overset{\overset{C_6H_5}{|}}{CH}CH_2CH_3 \tag{1}$$
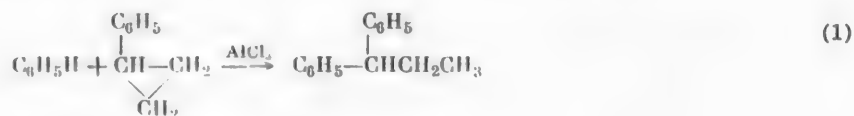
The structure of this alkylation product was shown by its counter synthesis — by the reduction of 1,1-diphenyl-1-propene with sodium in butyl alcohol.

$$(C_6H_5)_2C=CHCH_3 \xrightarrow{+H_2} (C_6H_5)_2CHCH_2CH_3 \tag{2}$$

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* It would seem quite possible that the alkylation goes in two stages, i.e. that the arylcyclopropanes are first isomerized by aluminum chloride to arylpropenes (propenylbenzenes), which then react further in the alkylation. To check this theory we examined the possibility of alkylating benzene with propenylbenzene under the adopted conditions (in the presence of aluminum chloride; 0-10°). It proved that the propenylbenzene suffered complete polymerization during reaction. Consequently, the theory that to obtain the alkylation product of benzene necessitates the presence of propenylbenzene, and not of phenylcyclopropane, was refuted.

The two different 1,1-diphenylpropane preparations, having the same constants, were identified by preparing the crystalline monoacetyl derivative (the mixed melting point of the two acetyl derivatives was not depressed).

$$\begin{array}{c} C_6H_5 \\ C_6H_5 \end{array}\!\!\!>\!\!CHCH_2CH_3 + CH_3COCl \xrightarrow{AlCl_3} \begin{array}{c} p\text{-}CH_3COC_6H_4 \\ C_6H_5 \end{array}\!\!\!>\!\!CHCH_2CH_3$$

Consequently, it was established that the alkylation of benzene with phenylcyclopropane in the presence of aluminum chloride leads to the formation of 1,1-diphenylpropane, in the same manner as the reaction of benzene with styrene under similar conditions yields 1,1-diphenylethane [13, 14].

The lowest yield of alkylation product, of 1,1-diarylpropane, was obtained in the case of alkylating benzene with phenylcyclopropane (52% yield), which increased on going to toluene (61.5%) and anisole (72.5%), this being due to the greater mobility of the hydrogen atoms (in the para position) in toluene and anisole.

$$p\text{-}XC_6H_4H + \overset{C_6H_5}{\underset{CH_2}{\overset{|}{CH}\!\!-\!\!CH_2}} \longrightarrow p\text{-}XC_6H_4\!\!-\!\!\overset{C_6H_5}{\overset{|}{CH}}CHCH_2CH_3 \tag{3}$$

$$X = CH_3 \text{ and } CH_3O.$$
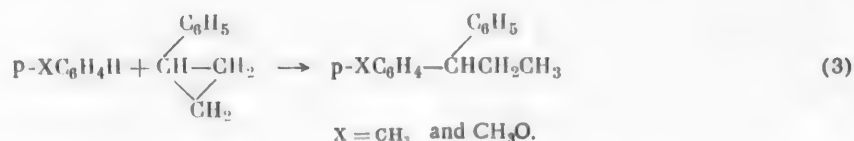
In alkylating toluene and anisole the substitution could be in either the para or the ortho position; it was shown by counter synthesis that the alkylation products are respectively 1-phenyl-1-p-tolylpropane and 1-phenyl-1-p-anisylpropane. In the counter synthesis of these compounds we used a method that excluded any doubt as to the position of the substituents (CH_3 or CH_3O group), namely the alkylation of benzene with p-tolyl- and p-anisylcyclopropane.

$$C_6H_5H + \overset{p\text{-}XC_6H_4}{\underset{CH_2}{\overset{|}{CH}\!\!-\!\!CH_2}} \xrightarrow{AlCl_3} C_6H_5\!\!-\!\!\overset{p\text{-}XC_6H_4}{\overset{|}{CH}}CHCH_2CH_3 \tag{4}$$

$$\text{where } X = CH_3 \text{ and } CH_3O.$$
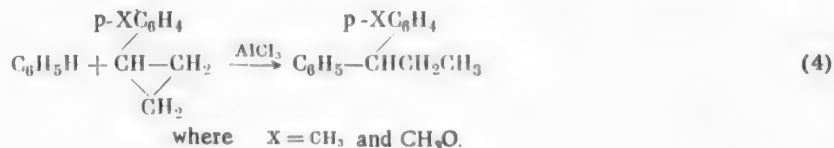
The diarylpropanes, obtained according to equations (3) and (4), were characterized by preparing the crystalline monoacetyl derivatives. The identity of the corresponding monoacetyl derivatives was established by their same melting point and by the absence of a mixed melting-point depression. Consequently, it was established that toluene and anisole are alkylated by arylcyclopropanes (equation 3) only in the para position.

The alkylation of benzene with either p-tolyl or p-anisyl-cyclopropane (equation 4) does not go as smoothly as when phenylcyclopropane is used. The yield of 1,1-diarylpropane is 34% when alkylation is with p-tolyl-cyclopropane, and only 5.5% when the alkylation is with p-anisylcyclopropane; the reduced yield here was due to the polymerization of the arylcyclopropanes by the aluminum chloride. The tendency of arylcyclopropanes to polymerize, already quite noticeable when p-tolylcyclopropane is used and predominating in the case of p-anisylcyclopropane, is apparently due to the influence of the nucleophilic substituents (CH_3, CH_3O) found in the benzene ring.

EXPERIMENTAL

The starting arylcyclopropanes were obtained by the Kizhner method, i.e. by the decomposition of the corresponding pyrazoline bases, and were freed of isomeric arylpropenes by treatment with potassium permanganate [6]. After distillation through a column (40 theoretical plates) the arylcyclopropanes had the following constants:

Phenylcyclopropane — b.p. 172.5-173° (745 mm), n_D^{20} 1.5336, d_4^{20} 0.9420, MR_D 38.98. C_9H_{10} F 3 Δ. Calculated 38.67, EM_D 0.31.

p-Tolylcyclopropane — b.p. 194-194.5° (745 mm), n_D^{20} 1.5241, d_4^{20} 0.9227, MR_D 43.82. $C_{10}H_{12}$ F 3 Δ. Calculated 43.29, EM_D 0.53.

p-Anisylcyclopropane — b.p. 223.5-224° (747 mm), n_D^{20} 1.5319. d_4^{20} 1.0018, MR_D 45.82. $C_{10}H_{12}O$ F 3 Δ. Calculated 44.92, EM_D 0.90.

Alkylation of benzene with phenylcyclopropane in the presence of aluminum chloride. Phenylcyclopropane (36.5 g; 0.3 mole) was added very slowly in drops to a mixture of 78 g (1 mole) of benzene and 12 g (0.09 mole) of aluminum chloride with stirring and cooling (the temperature was maintained at 0-10°). Then the reaction mixture was stirred for 5 hours at room temperature, and the next day it was treated with water. The benzene layer was combined with the benzene extracts of the water layer and the whole then washed successively with 2N hydrochloric acid, water, soda and again with water, and finally it was dried over calcium chloride. The residue after distilling off the benzene was vacuum-distilled. The yield of 1,1-diphenylpropane was 30 g (52%).

B.p. 139° (10 mm), n_D^{20} 1.5645, d_4^{20} 0.9873, MR_D 64.71. $C_{15}H_{16}$ F 6. Calculated 64.27, EM_D 0.44.

Found %: C 91.60, 91.61; H 8.36, 8.30. $C_{15}H_{16}$. Calculated %: C 91.83; H 8.17.

Literature [15] : b.p. 139° (11 mm), n_D^{20} 1.5657, d_4^{20} 0.9919, MR_D 64.53.

Counter synthesis of 1, 1-diphenylpropane. Thirty grams of sodium metal (one piece) was added to a solution of 34 g of 1,1-diphenyl-1-propene (obtained by the dehydration of ethyldiphenylpropane with potassium bisulfate; m.p. 51-52°; according to [15], m p. 52°) in 470 ml of anhydrous butyl alcohol, and then the flask was immediately placed in an oil bath previously heated to 180°. When reaction was ended, the reaction mixture was treated with water. The solution of diphenylpropane in butyl alcohol was separated and dried; the residue after distilling off the butyl alcohol was vacuum-distilled. The yield of 1,1-diphenylpropane was 24 g (74%).

B.p. 135-136° (7 mm), n_D^{20} 1.5640, d_4^{20} 0.9864, MR_D 64.72. $C_{15}H_{16}F_6$. Calculated 64.27, EM_D 0.45.

Acetyl derivatives from the two 1,1-diphenylpropane preparations. To a solution of 6.6 g (0.05 mole) of aluminum chloride in 50 ml of dry carbon tetrachoride was first added 3.9 g (0.05 mole) of acetyl chloride, and then 9.8 g (0.05 mole) of diphenylpropane in 15 ml of carbon tetrachloride (the reaction was run with constant stirring; the temperature of the reaction mixture was maintained at about 2°). After 4 hours the mixture was treated in succession with 2N hydrochloric acid, soda solution, and water. The residue after distilling off the carbon tetrachloride was vacuum-distilled. The 1-phenyl-1-p-acetophenylpropane (new in the literature) obtained from each 1,1-diphenylpropane specimen (in 42% yield) had the same m.p. of 75-77°; the mixed melting point of the two preparations was not depressed.

Found %: C 85.51, 85.51; H 7.52, 7.68. $C_{17}H_{18}O$. Calculated %: C 85.71; H 7.56.

Alkylation of toluene with phenylcyclopropane in the presence of aluminum chloride. The reaction was run in the same manner as described for the alkylation of benzene with phenylcyclopropane and led to obtaining 1-phenyl-1-p-tolylpropane in 61.5% yield (the compound is new).

B.p. 146° (7 mm), n_D^{20} 1.5589, d_4^{20} 0.9773, MR_D 69.47. $C_{16}H_{18}$ F 6. Calculated 68.88, EM_D 0.59.

Found %: C 91.33, 91.35; H 8.78, 8.80. $C_{16}H_{18}$. Calculated %: C 91.42; H 8.58.

The product obtained by the monoacylation of 1-phenyl-1-p-tolylpropane with acetyl chloride in the presence of aluminum chloride had m.p. 64-65° (the compound is new).

Found %: C 85.72, 85.34; H 7.77, 7.71. $C_{18}H_{20}O$. Calculated %: C 85.72; H 7.93.

Counter synthesis of 1-phenyl-1-p-tolylpropane. The alkylation of benzene with p-tolylcyclopropane led to obtaining 1-phenyl-1-p-tolylpropane in a smaller yield (34%), having exactly the same constants as the product described above.

B.p. 145-146° (7 mm), n_D^{20} 1.5588, d_4^{20} 0.9782, MR_D 69.39. $C_{16}H_{18}$ F 6. Calculated 68.88, EM_D 0.51.

The monoacetyl derivative obtained from this 1-phenyl-1-p-tolylpropane specimen also had m.p. 64-65°; the mixed melting point of the two specimens of this derivative was not depressed.

Alkylation of anisole   with phenylcyclopropane in the presence of aluminum chloride.   The alkylation product obtained here was 1-phenyl-1-p-anisylpropane (72.5% yield;   new in the literature).

B.p. 168° (7 mm), n_D^{20} 1.5662, d_4^{20} 1.0357, MR_D 71.29. $C_{16}H_{18}OF_6$. Calculated 70.53. EM_D 0.76.

Found % C 85.20, 85.36; H 8.19, 8.20. $C_{16}H_{18}O$. Calculated % C 84.95; H 7.97.

The monoacetyl derivative (also new in the literature) had m.p. 66-67°.

Found %: C 80.98, 80.90, H 7.78, 7.74. $C_{18}H_{20}O_2$. Calculated %: C 80.60; H 7.46.

Counter synthesis of 1-phenyl-1-p-anisylpropane.   The alkylation of benzene with p-anisylcyclopropane,having constants close to those of the product described above.

B.p. 168° (7 mm), n_D^{20} 1.5641, d_4^{20} 1.0365, MR_D 71.13. $C_{16}H_{18}OF_6$. Calculated 70.53, EM_D 0.60.

The monoacetyl derivative had m.p. 66-67°; the mixed melting point of the two preparations was not depressed.

Attempted alkylation of benzene with propenylbenzene in the presence of aluminum chloride. Propenylbenzene (b.p. 175-175.5° for 747 mm, n_D^{20} 1.5480, d_4^{20} 0.9122;according to [16]: b.p. 174.5-175.5°, n_D^{20} 1.5475, d_4^{20} 0.9125) was reacted with benzene in the presence of aluminum chloride under the same conditions as were used to alkylate benzene with phenylcyclopropane (at 0-10°); here the propenylbenzene polymerized completely and an alkylation product could not be isolated.

SUMMARY

1. We were the first to study the alkylation of the aromatic ring with arylcyclopropanes. It was found that the alkylation of benzene, toluene and anisole with phenylcyclopropane in the presence of aluminum chloride leads to cleavage of the three-membered ring and the formation of 1-phenyl-1-arylpropanes (in a yield of 52, 61.5 and 72.5%, respectively).

2. It was shown that toluene and anisole are alkylated by phenylcyclopropane in the para position.

3. It was established that the alkylation of benzene with p-tolylcyclopropane and p-anisylcyclopropane proceeds less smoothly (the yields of the corresponding 1,1-diphenylarylpropanes are 34 and 5.5%, respectively) than in the case of phenylcyclopropane, since p-tolylcyclopropane, and especially p-anisylcyclopropane, suffer substantial polymerization in the presence of aluminum chloride.

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SYNTHESIS OF $C_{14} - C_{20}$ ALKYLBENZENES BY GRIGNARD-WURTZ REACTION IN ETHER-FREE MEDIUM

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In a previous study [1] it was established that if the Grignard-Wurtz reaction between certain arylmagnesium halides and tertiary alkyl chlorides is run in n-heptane at 30-33° the yield of normal condensation products— alkylbenzenes— is increased several times when compared to the yield obtained when the same reaction is run in ether medium. In this paper, utilizing the above-described method, we reacted benzylmagnesium chloride with a number of branched-chain tertiary chlorides and obtained the following hydrocarbons.
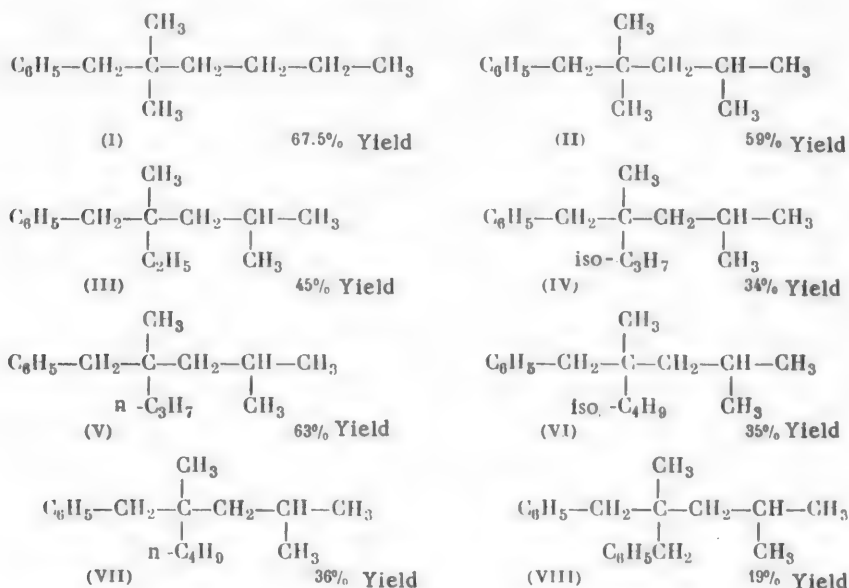
The fact that comparatively high yields* of alkylbenzenes were obtained by us is evidence that the secondary reaction — dehydrochlorination of the branched-chain tertiary chloride, usually accompanying the Grignard-Wurtz reaction and reducing the yield of normal condensation product — is suppressed to a large degree here. All of the reactions were run at uniform temperatures, not exceeding 35°.

We used a number of chlorides (7 of 8 run) with a regular change in structure (IX) for the condensation with benzylmagnesium chloride.

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*A. Bygden [2], who reacted $C_6H_5CH_2MgCl$ with tert-C_4H_9Br in ether, obtained about a 40% yield of 2-methyl-2-benzylpropane.

$$CH_3-CH-CH_2-\underset{\underset{R}{|}}{\overset{\overset{CH_3}{|}}{C}}Cl, \quad \text{where} \quad R = CH_3, \ C_2H_5, \ iso\text{-}C_3H_7, \ n\text{-}C_3H_7, \\ iso\text{-}C_4H_9, \ n\text{-}C_4H_9, \ CH_2C_6H_5.$$

(IX)
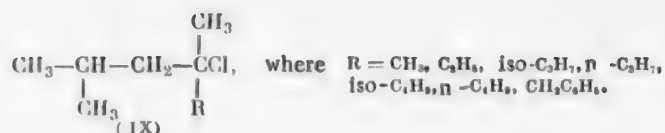
The highest yield (63%) was obtained using 4-chloro-2,4-dimethylheptane (R = n-C₃H₇). It is interesting to mention that in some recent studies by one of us and co-workers[3, 4] on the condensation of tertiary alkyl halides with allyl- and methallylmagnesium chlorides

$$CH_2{=}CH-CH_2Cl\ (CH_2{=}\underset{\underset{CH_3}{|}}{C}-CH_2Cl) + Mg + Cl-\underset{\underset{R}{|}}{\overset{\overset{CH_3}{|}}{C}}-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-CH_3 \xrightarrow{-MgCl_2} \text{1-alkene}$$

where R = CH₃, C₂H₅, n-C₃H₇, iso-C₄H₉, iso-C₅H₁₁
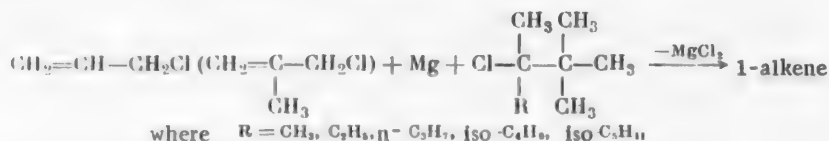
the maximum yields of hydrocarbons were obtained where R = n-C₃H₇ and iso-C₄H₉.

TABLE 1

Name of hydrocarbon	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D		Found (%)		Empirical formula	Calculated (%)	
				found	calculated •	C	H		C	H
2-Methyl-2-benzyl-hexane	111° (6)	1.4911	0.8717	63.14	63.40	88.52	11.67	C₁₄H₂₂	88.42	11.58
2,4-Dimethyl-2-benzyl-pentane	86 (0.5)	1.4930	0.8700	63.13	63.44	88.36	11.61	C₁₄H₂₂	88.42	11.58
3,5-Dimethyl-3-benzyl-hexane	97 (0.5)	1.4959	0.8888	67.62	67.83	88.62	11.45	C₁₅H₂₄	88.16	11.84
2,3,5-Trimethyl-3-benzyl-hexane	107—108.5 (1.5)	1.5034	0.8933	72.12	72.26	88.30	11.62	C₁₆H₂₆	88.00	12.00
2,4-Dimethyl-4-benzyl-heptane	111.5 (3)	1.4970	0.8811	72.52	72.47	87.76	11.76	C₁₆H₂₆	88.00	12.00
2,4,6-Trimethyl-4-benzylheptane	133—135 (5)	1.5005	0.8868	76.93	77.15	88.11	11.74	C₁₇H₂₈	87.86	12.14
2,4-Dimethyl-4-benzyl-octane	150.5—151.5 (6)	1.4989	0.8833	77.24	77.12	88.06	11.85	C₁₇H₂₈	87.86	12.14
2-Methyl-4,4-dibenzyl pentene	178—180 (7)	1.5447	0.9604	87.67	87.60	90.48	9.75	C₂₀H₂₆	90.15	9.85

•By the V. M. Tatevskii method [18].

The results obtained by us permit making some conclusions relative to the relationship between the structure of the starting compounds and the yield of reaction product — the corresponding alkylbenzene. First of all, it should be mentioned that a monotonic increase or decrease in the yields of alkylbenzenes with a regular change in one of the radicals of the tertiary chloride in the series CH₃, C₂H₅, iso-C₃H₇, n-C₄H₉, etc. is absent (which might be expected if the remainder of the molecule was kept constant). As is known, the induction effect of the

50

alkyl group increases in the indicated series, which should facilitate condensation. On the other hand, both the molecular weight and the degree of branching of the radicals increase in the indicated series, and this increase in the steric hindrance causes a reduction in the yield of hydrocarbons in the Grignard-Wurtz reaction. Consequently, the variation in the yields obtained by us must be attributed to the simultaneous influence exerted by at least the two mentioned factors. Together with this, a regular alternation in the yields of hydrocarbons in the series (II, III, V, VII) (R= CH_3, C_2H_5, n-C_3H_7, n-C_4H_9) lends support to the theory that in the present case we have an alternate increase and decrease in the reactivity of the tertiary chlorides in this series that is independent of the influence exerted by the above-discussed factors. Such an alternation in the properties of the halides is apparently linked with the presence or absence of conjugation between the C—Cl and C—H bonds (σ,σ-conjugation) in the halide molecule. As we had shown earlier [4], when such conjugation is present the reactivity of saturated alkyl halides approaches that of halides with σ, π-conjugation.

EXPERIMENTAL

2-Methyl-2-benzylhexane (I). An ether solution of 157 g of acetone was added to the Grignard reagent prepared from 80.5 g of magnesium and 411 g of butyl bromide in 2 liters of absolute ether. After the conventional workup we obtained 220 g of 2-methyl-2-hexanol.

B.p. 60-61° (35mm), n_D^{20} 1.4170, d_4^{20} 0.8153. From [5] : b.p. 139.4-140° for 735 mm, n_D^{20} 1.4175, d_4^{20} 0.8119.

The alcohol was treated with dry HCl at 0° (all of the other chlorides were obtained in a similar manner). We obtained 226 g of 2-chloro-2-methylhexane:

B.p. 59.5° (52 mm), n_D^{20} 1.4200, d_4^{20} 0.8635, MR_D 39.46; calc. 39.39. From [6]: B.p. 76.2-76.4° (103 mm), n_D^{25} 1.4185.

An ether solution of benzylmagnesium chloride (from 80 g of magnesium and 157 g of benzyl chloride) was filtered under nitrogen into a three-necked flask, fitted with stirrer, dropping funnel and reflux condenser. The ether was distilled off at atmospheric pressure, and the residue was treated with 500 ml of dry n-heptane. A solution of 135 g of 2-chloro-2-methylhexane in 150 ml of heptane was added in 6 hours, with vigorous stirring, to the obtained suspension. The temperature in the flask was kept below 35° by external cooling of the flask. Then the reaction mixture was stirred for another 8 hours, after which it was decomposed with 5% hydrochloric acid solution. The solvent was distilled off, and the residue was distilled twice from sodium. We obtained 69 g (27.5%) of 2-methyl-2-benzyl -2-benzylhexane. The properties of all of the alkylbenzenes synthesized by us are given in Table 1.

2,4-Dimethyl-2-benzylpentane (II). The reaction of methylmagnesium bromide with methyl isobutyl ketone gave a 77% yield of 2,4-dimethyl-2-pentanol.

B.p. 59.5° (42.5 mm), n_D^{20} 1.4170, d_4^{20} 0.8119. From [7]: b.p. 133° (749 mm), n_D^{20} 1.4172, d_4^{20} 0.8158.

The hydrochlorination of the alcohol gave 2-chloro-2,4-dimethylpentane:

B.p. 46° (44 mm), n_D^{20} 1.4182, d_4^{20} 0.8628, MR_D 39.32; calc. 39.39. From [8]: B.p. 33-34° (20 mm), n_D^{15} 1.4239.

The chloride (101 g) was reacted with the Grignard reagent, prepared from 60.8 g of magnesium and 167.1 g of benzyl chloride, under conditions similar to those given above. We obtained 84 g (59%) of 2,4-dimethyl-2-benzylpentane.

3,5-Dimethyl-3-benzylhexane (III). The Grignard reaction of 76 g of magnesium, 468 g of ethyl iodide and 270 g of methyl isobutyl ketone gave 210 g (59%) of 3,5-dimethyl-3-hexanol.

B.p. 54° (14.5 mm), n_D^{20} 1.4264, d_4^{20} 0.8261. From [9]: b.p. 151° (768) mm, n_D^{18} 1.4286, d^{15} 0.830.

The alcohol was converted to 3-chloro-3,5-dimethylhexane:

B.p. 40.5° (13 mm), n_D^{20} 1.4298, d_4^{20} 0.8747, MR_D 43.88; calc. 44.01.

Using the conditions described above, 60.9 g of the chloride was reacted with the benzylmagnesium chloride obtained from 18.6 g (45%) of 3,5-dimethyl-3-benzylhexane.

<u>2,3,5-Trimethyl-3-benzylhexane (IV)</u>. An ether solution of 180 g of methyl isobutyl ketone was added in 2 hours at a reaction temperature not exceeding - 30° to the isopropyllithium obtained from 31 g of lithium and 163 g of isopropyl chloride in ether at − 35° [10]. Stirring at -30° was continued for another 1.5 hours, after which the flask contents were poured on ice (the unreacted lithium was first removed by filtration). The ether solution was dried over anhydrous Na_2SO_4, the solvent removed, and the residue fractionally distilled to give 70.3 g (29%) of 2,3,5-trimethyl-3-hexanol.

B.p. 52-54° (7 mm), n_D^{20} 1.4292, d_4^{20} 0.8312. From [11]: b.p. 45.3° (3 mm), n_D^{20} 1.4321.

The alcohol was converted to 3-chloro-2,3,5-trimethylhexane, which had:

B.p. 55-55.5° (7 mm), n_D^{20} 1.4371, d_4^{20} 0.8794, MR_D 48.48; calc. 48.63.

The reaction of 48.5 g of 3-chloro-2,3,5-trimethylhexane with benzylmagnesium chloride (from 12.5 g of magnesium and 45 g of benzyl chloride in 300 ml of heptane) gave 17 g (34%) of 2,3,5-trimethyl-3-benzyl-hexane.

<u>2,4-Dimethyl-4-benzylheptane (V)</u>. 2,4-Dimethyl-4-pentanol was obtained in 70% yield from 54 g of magnesium, 246 g of propyl bromide and 180 g of methyl isobutyl ketone.

B.p. 67° (6 mm), n_D^{20} 1.4297, d_4^{20} 0.8242. From [12]: B.p. 79° (26 mm), n_D^{20} 1.4298, d_4^{20} 0.8254.

The alcohol was converted to 4-chloro-2,4-dimethylheptane, which had:

B.p. 65° (13 mm), n_D^{20} 1.4320, d_4^{20} 0.8672, MR_D 48.77; calc. 48.63.

The Grignard reaction of the chloride (59.6 g) with benzylmagnesium chloride (from 18.6 g of magnesium and 76 g of benzyl chloride in 300 ml of n-heptane) gave 59.5 g (63%) of 2,4-dimethyl-4-benzylheptane.

<u>2,4,6-Trimethyl-4-benzylheptane (VI)</u>. Isobutyllithium [13] was obtained in 65% yield from 15.3 g of lithium and 92.6 g of isobutyl chloride in isopentane. A solution of 75 g of methyl isobutyl ketone in 150 ml of isopentane was added in 4 hours to the boiling solution of isobutyllithium. After removing the pieces of lithium, the reaction mixture was poured on ice. After the usual workup and fractionation we obtained 52 g (43%) of 2,4,6-trimethyl-4-pentanol:

B.p. 94-96° (25 mm), n_D^{20} 1.4319, d_4^{20} 0.8241. From [14]: b.p. 180-182° (753 mm), n_D^{18} 1.4334, d^{20} 0.823.

The alcohol was shaken with an equal volume (two portions) of concentrated hydrochloric acid at 5-10° for 2 hours. After drying over anhydrous $CaCl_2$ the hydrochlorination product was blown with a stream of dry nitrogen for 4 hours to remove excess HCl, and then it was fractionally distilled in vacuo. A wide fraction was collected for further synthesis.

B.p. 55-66° for 14.5 min, n_D^{20} 1.4309-1.4366, d_4^{20} 0.8605.

Found %: Cl 8.14. $C_{10}H_{21}Cl$. Calculated %: Cl 20.06; amount of 4-chloro-2,4,6-trimethylheptane 40.6%.

From [3]: the hydrochlorination of methyldiisobutylcarbinol with dry HCl at 0° yields only 3% of the chloride, while at 70° the yield of the chloride is 10%, b.p. 72-73° (13 mm), n_D^{20} 1.4355, d_4^{20} 0.8677. From [15]: b.p. 82-83° (25 mm), n_D^{15} 1.43336, d_4^{20} 0.8657.

We took 25.7 g of 4-chloro-2,4,6-trimethylheptane (calculated amount of 100% chloride) to react with benzylmagnesium chloride (from 24.3 g of magnesium and 90 g of benzyl chloride in 300 ml of n-heptane). The reaction product contained, besides the usual impurities of toluene and olefin (corresponding to the tertiary chloride), also dibenzyl with m.p. 51.5-52°, which we were able to isolate by cooling the fraction with b.p. 137-147° (15 mm) to -50°. After purification we obtained 12 g (35%) of 2,4,6-trimethyl-4-benzylheptane.

<u>2,4-Dimethyl-4-benzyloctane (VII)</u>. An ether solution of 110 g of methyl isobutyl ketone was added (with cooling of the reaction flask by ice water) in 5 hours to a solution of butyllithium [16], prepared from 19 g of lithium and 180 g of butyl bromide in ether. After the usual workup we isolated 110 g (64%) of 2,4-dimethyl-4-octanol, b.p. 73.5-75° (5 mm), n_D^{20} 1.4325, d_4^{20} 0.8227. The hydrochlorination product of the alcohol (dry HCl at 0°) had:

B.p. 82-84° (7 mm), n_D^{20} 1.4371, d_4^{20} 0.8680.

Found %: Cl 16.1. $C_{10}H_{21}Cl$. Calculated %: Cl 20.06.

TABLE 2

Name of hydrocarbon	Boiling point (pressure in mm)	Freezing point •	n_D^{20}	d_4^{20}	found (%)		Empirical formula	calculated (%)		v_{20} (centistokes)	Q_H •• (Kcal/kg)
					C	H		C	H		
2,2-Dimethyl-1-cyclohexyl-pentane	87° (3)	−80°	1.4540	0.8262	85.57	14.47	$C_{14}H_{28}$	85.63	14.37	3.36	10370
2,2,4-Tri-methyl-1-cyclohexyl-pentane	95 (5)	−114	1.4561	0.8233	85.60	14.27	$C_{14}H_{28}$	85.63	14.37	3.27	10419
2,4-Dimethyl-2-ethyl-1-cyclohexyl-pentane	126 (8)	−76	1.4641	0.8445	85.30	14.48	$C_{15}H_{30}$	85.63	14.37	5.35	10416
2,4-Dimethyl-2-isopropyl-1-cyclohexyl-pentane.	123 (6)	−78	1.4638	0.8438	85.42	14.50	$C_{16}H_{32}$	85.63	14.37	6.82	10380
2,4-Dimethyl-2-propyl-1-cyclohexyl-pentane	127 (5)	−83	1.4620	0.8368	85.83	14.31	$C_{16}H_{32}$	85.63	14.37	5.45	10420
2,4-Dimethyl-2-isobutyl-1-cyclohexyl-pentane	133—135 (7.5)	−82	1.4604	0.8384	85.93	14.00	$C_{17}H_{34}$	85.63	14.37	5.74	10462
2,4-Dimethyl-2-butyl-1-cyclohexyl-pentane	113—114 (1)	−68	1.4619	0.8382	85.54	14.23	$C_{17}H_{34}$	85.63	14.37	9.10	10320
2-Methyl-2-isobutyl-1,3-dicyclohexyl-propane	204 (12)	−45	1.4814	0.8820	86.03	13.85	$C_{20}H_{38}$	86.25	13.75	47.56	10385

• All of the hydrocarbons congealed as glasses; GOST 1533-42 was used to determine the freezing points.

•• GOST 5080-55 was used to determine the heat-generation capacity by combustion in a calorimetric bomb.

The hydrochlorination product (121.7 g), containing 80.2% 4-chloro-2,4-dimethyloctane, was reacted with benzylmagnesium chloride (from 24.3 g of magnesium and 96 g of benzyl chloride in 400 ml of heptane). After freezing out the dibenzyl we obtained 40.2 g (34%)of 2,4-dimethyl-4-benzyloctane.

2-Methyl-4,4-dibenzylpentane. 2-Methyl-4-benzyl-4-pentanol was obtained from 51 g of magnesium, 253 g of benzyl chloride and 180 g of methyl isobutyl ketone in 2 liters of ether.

B.p. 93-94.5° (1.5 mm), n_D^{20} 1.5054, d_4^{20} 0.9435. From [17]: yield 62%, properties not given.

The hydrochlorination product (using dry HCl at 0°) decomposes when vacuum-distilled (4 mm). After a second treatment with hydrogen chloride for 5 hours, followed by removal of excess HCl, the product was analyzed for its chlorine content.

Found %: Cl 5.49. $C_{13}H_{19}Cl$. Calculated %: Cl 16.83.

The compound (138 g) (a mixture of chloride and olefin), containing 33% 4-chloro-2-methyl-4-benzyl-pentane, was reacted with the Grignard reagent prepared from 12 g of magnesium and 44.5 g of benzyl chloride in 300 ml of heptane. After purification we obtained 10 g (18.8%) of 2-methyl-4,4-dibenzylpentane.

All of the alkylbenzenes were hydrogenated to the corresponding alkylcyclohexanes over Ni catalyst, using a hydrogen pressure of 120-150 atm and a temperature of 180-200°. The properties of the hydrogenation products are listed in Table 2.

SUMMARY

1. Eight new alkylbenzenes were synthesized by running the Grignard-Wurtz reaction in heptane, which on hydrogenation gave the corresponding alkylcyclohexanes. The fact that the alkylbenzenes were obtained in high yields (up to 67%) supports the practicality of replacing ether by a hydrocarbon solvent in the second stage of the reaction.

2. It was shown that the yields of hydrocarbons in the given reaction also depend to a large degree on whether σ,σ-conjugation of the C—Cl and C—H bonds in the original alkyl halide is present or absent, this being determined by the structure of the radical.

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ELECTROREDUCTION OF PEPTIDES OF PROLINE AND OF
DIALKYLAMIDES OF AMINO ACIDS

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In previous papers one of us [1] had shown that diketopiperazines when subjected to electroreduction are converted to piperazines, whereas both peptides and amino acids (except cystine) remain unchanged under these conditions. In addition, it was shown that the dialkylamides of aromatic acids (I) are also easily reduced by an electric current. The reduction products were not investigated by the authors.

Peptides of proline (II), in which the imino group of proline is present as a peptide linkage, may be regarded as being dialkylamides of amino acids.
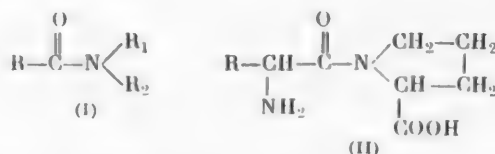
Consequently it could be expected that peptides of proline would also be reduced when subjected to electroreduction under the adopted conditions. We investigated the electroreduction of a number of proline peptides, and also of some compounds of a peptide character, containing the dialkylamido grouping. The following peptides were reduced: glycyl-L-proline, glycyl-D,L-valine and D,L-phenylalanyl-D,L-proline methyl ester hydrochloride. We also reduced the following amino acid dialkylamides: glycine α-methylpyrrolide, glycine diethylamide, glycine piperidide, D,L-phenylalanine piperidide and D, L-leucine piperazide. All of the enumerated compounds reduce in such manner that the amino alcohol is formed from the amino acid in which the carboxyl group is present as a peptide linkage, and the corresponding dialkylamine (proline, α-methylpyrrolidine, diethylamine, piperidine, piperazine) is liberated, in accordance with the following scheme:
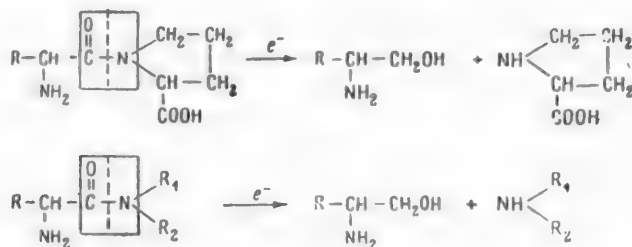
Here it is important that the nature of the amino acid does not affect the structure of the final reduction products, since the corresponding amino alcohols were found in all of the cases, and were either isolated or identified chromatographically.

The method described in [2] was used to run the electroreductions. The weight of substance taken did not exceed 100 mg. The cathode solution was composed of 50 ml of acetic acid, 100 ml of water and 40 ml of 22% distilled HCl. The anode compartment contained 70 ml of 5% HCl. The current density was 56 μa per sq.cm, the cathode temperature 15-20°, and the reduction time 5-7 hours. The direct current used was 120 v. The cathode solutions were investigated using paper chromatography and the solvent system butanol-water-acetic acid (4:5:1). At the same time we also resorted to ionophoresis on paper. As buffer we used 30% acetic acid, and the potential gradient was 6.8 v/cm. To develop the chromatograms and ionophoregrams we used either a 0.4% solution of ninhydrin in methanol at 100° or benzidine.

D,L-Phenylalanine piperidide hydrochloride. a) The cathode solution after reduction and evaporation was chromatographed. When benzidine was used for developing,the obtained stains had distribution coefficients $R_f = 0.47$, $R_f = 0.59$ (very small) and $R_f = 0.67$, which in the control corresponds to piperidine ($R_f = 0.47$), phenyl-alanine ($R_f = 0.59$) and phenylalaninol (β-benzyl-β-aminoethanol; $R_f = 0.67$).

b) The cathode solution after evaporation and removal of excess HCl was dissolved in 5 ml of water, made alkaline with 1 drop of conc. NaOH, and extracted several times with methylene chloride. The methylene chloride was evaporated in vacuo. The residual oil with a sharp amine odor proved to be chromatographically homogeneous and had $R_f = 0.67$. The substance was dissolved in 1 ml of anhydrous ethanol saturated with HCl, and then 10 ml of absolute ether was added. The white glistening crystals that deposited here were filtered and washed with absolute ether. Weight 15 mg, m.p. 145-146°. D,L-Phenylalaninol hydrochloride, obtained by the reduction of D,L-phenylalanine with LiAlH$_4$, has m.p. 144-145°. The mixed melting point of the two specimens was not depressed. According to [3], D,L-phenylalaninol hydrochloride has m.p. 145-147°. When treated with sodium periodate,the substance cleaves ammonia, which was detected with Nessler reagent, this being a specific test for α-amino alcohols.

Glycyl-L-proline. a) Here 60 mg of the peptide was taken and reduced for 5 hours. The cathode solution after the reduction was evaporated in vacuo, and the residue was hydrolyzed for 6 hours with 22% HCl to remove the starting peptide. The hydrolyzate was evaporated in vacuo, and the residue was dissolved in 0.5 ml of water and chromatographed. When ninhydrin was used for developing,the obtained stains had distribution coefficients $R_f = 0.14$ (small), $R_f = 0.31$ and $R_f = 0.40$ (yellow), which in the control corresponds to glycine ($R_f = 0.14$), ethanolamine ($R_f = 0.31$) and proline ($R_f = 0.40$, yellow). Using ionophoresis on paper (4 hours) and ninhydrin the developer led to obtaining three stains, localized on the cathode at 5.5 (yellow), 8.5 (small) and 11 cm. The first two stains correspond to proline and glycine, while the third corresponds to ethanolamine (in the control the ethanolamine was located on the cathode at 11 cm).

b) Azeotropic distillation of ethanolamine with toluene. To separate ethanolamine we used the method of [4], which is based on the ability of toluene to form an azeotropic mixture with ethanolamine. The experiment was run in a liquid extractor suitable for the extraction of a light liquid. The hydrolyzate of the reduced glycyl-L-proline, after removal of the HCl, was transferred to the extraction flask, and then 3 ml of saturated aqueous potash solution and 50 ml of toluene (washed with HCl and distilled) were added. The extraction flask was then filled with water so that its level was approximately 2 cm below the outlet tube. The toluene and substance in the flask were boiled for 7 hours. The azeotropic mixture condensed in the condenser, dropped into the funnel of the extractor, and then passed through a layer of water; here the ethanolamine dissolved in the water, while the toluene flowed back into the extraction flask through the outlet tube. The water layer was separated and then evaporated in vacuo at 40° to a volume of 7 ml. The concentrate gave an intense ninhydrin test and was free of ammonia (using Nessler reagent). Chromatographing of the indicated water solution revealed the presence of only one substance, with $R_f = 0.41$. In the control experiment the ethanolamine had $R_f = 0.41$. Ionophoresis also revealed only one substance, migrating to the cathode at the speed of ethanolamine. Titration of the indicated concentrate with 0.01N HCl, using a microburet and universal indicator, gave 0.16 mg of N in 1 ml of concentrated, while by the periodate method [5] the found amount was 0.15 mg of N, determined as ammonia.

D,L-Valyl-D,L-proline. Here 50 mg of the peptide was reduced under the above-described conditions for 5 hours. The cathode solution was evaporated, and the residue was dissolved in 1 ml of water and chromatographed. It proved that valine, valinol (β-isopropyl-β-aminoethanol) and the starting peptide do not separate in the given

solvent system. To separate from amino acid and peptide, the obtained solution was made alkaline with 5 ml of 2N NaOH and then extracted several times with ether. The ether extract was evaporated to dryness. The residue, a small amount of oil with a sharp amine odor, was dissolved in 1 drop of alcohol and chromatographed. When developed with benzidine only one stain appeared with $R_f = 0.67$. In this experiment the valinol control had $R_f = 0.67$.

D, L-Phenylalanyl-D,L-proline methyl ester hydrochloride. Here 100 mg of the hydrochloride was reduced by the above-described method. The cathode solution, after reduction and distilling off the solvent, was hydrolyzed for 12 hours with 22% HCl, then evaporated to dryness, and the residue dissolved in several drops of water and chromatographed. The investigated solution was found to contain proline, a minute amount of phenylalanine and a new substance, from the distribution coefficient ($R_f = 0.70$) corresponding to β-benzyl-β-aminoethanol (phenylalaninol). The phenylalaninol in the control had $R_f = 0.70$. The investigated solution was made alkaline with 2N NaOH and then extracted 3 times with 5 ml portions of chloroform, after which the chloroform was distilled off and the residue was chromatographed. With either ninhydrin or benzidine the substance developed only one stain, from its distribution coefficient corresponding to phenylalaninol. The alkaline extract was devoid of ammonia, but on treatment with sodium periodate cleaved ammonia, which was detected with Nessler reagent (qualitative test for α-amino alcohols).

Glycine piperidide hydrochloride. The cathode solution, after reduction and distilling off the solvent, was chromatographed (using benzidine as developer) and found to contain substances with $R_f = 0.34$ and 0.56. Based on the control, this corresponds to ethanolamine ($R_f = 0.34$) and piperidine ($R_f = 0.56$.). In this experiment the glycine had $R_f = 0.1$, while the original had 0.65.

Glycine diethylamide. It was shown by chromatographing, that the hydrolyzate of the cathode solution after reduction contains substances with the distribution coefficients $R_f = 0.16$, 0.24 and 0.46 (small), and also several faint stains, the nature of which we were unable to establish. Based on the control, the indicated substances correspond to glycine ($R_f = 0.15$), ethanolamine ($R_f = 0.24$ and diethylamine ($R_f = 0.45$). Ionophoresis on paper (3 hours), using ninhydrin as developer, revealed the presence of glycine, ethanolamine and diethylamine. In addition, the cathode solution was found to contain ammonia, which was detected using Nessler reagent.

Glycine α-methylpyrrolidide hydrobromide. The cathode solution after reduction was found to contain substances with distribution coefficients $R_f = 0.15$ (small), 0.22 and 0.47. Based on the control, this corresponds to glycine ($R_f = 0.15$), ethanolamine ($R_f = 0.22$) and α-methylpyrrolidine ($R_f = 0.47$). The α-methylpyrrolidide in the control had $R_f = 0.57$.

D, L-Leucine piperazide dihydrobromide. Using benzidine as developer, the chromatograms of the hydrolyzate of the cathode solution after reduction revealed the presence of substances with distribution coefficients $R_f = 0.83$, 0.07 and 0.61 (traces). Based on the control, this corresponds to leucinol, piperazine and leucine.

SUMMARY

1. It was established that the electroreduction of peptides, employing the method of N. I. Gavrilov and A. V. Koperina, results in the reduction of the peptide linkage containing the imino group of proline.

2. The reduction of dialkylamides and piperazides of amino acids also occurs under the indicated conditions.

3. The electroreduction of proline peptides, and also of the piperazides and dialkylamides of amino acids, yields the amino alcohol derivatives of the corresponding amino acids. The nature of the amino acid does not affect either the character or the direction of the reduction.

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SYNTHESIS OF IODO DERIVATIVES OF BIPHENYL

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In previous studies [1-4] we had shown that some of the difficultly available aromatic iodo derivatives (due to the complexity of obtaining them) can be synthesized in good yield by direct iodination in the presence of nitration mixture ["mixed acid"]. Use of the latter results in complete utilization of the iodine, which is not lost as hydriodic acid during substitution. The mechanism of the direct iodination reaction in the presence of mixed acid has been discussed earlier [2,4]. The methods described in the literature [5] for the preparation of 4-iodo- and 4,4'-diiodobiphenyl through the corresponding diazonium compounds are both cumbersome and give low yields. A need for the indicated compounds led us, after the methods given in the literature for their preparation had been examined, to the present investigation, the results of which are given below.

EXPERIMENTAL

(Students É. M. Kulanova and L. A. Martynenko assisted in this portion of the work)

4-Iodobiphenyl.   To a mixture of 38.5 g of biphenyl, 100 ml of glacial acetic acid, 31.8 g of iodine and 27.5 ml of sulfuric acid (d 1.84), heated to 34-36° (bath temperature) in a round-bottomed flask, was gradually added in 1 hour 10 minutes, with vigorous mechanical stirring, 4.8 ml of nitric acid (d 1.4). Then the mixture was stirred for another 5 minutes. The reaction was then diluted with water, and the precipitate was filtered and washed. The precipitate had a brick-red color due to unreacted iodine. After steam distillation to remove iodine, the precipitate was recrystallized twice from ethanol. Yield of p-iodobiphenyl 45 g (64%); m.p. 113°. The qualitative test for nitrogen was negative.

Found %: I 45.40, 45.26. $C_{12}H_9I$. Calculated %: I 45.30.

4,4'-Diiodobiphenyl.   A mixture of 7.7 g of biphenyl, 12.7 g of iodine, 25 ml of glacial acetic acid and 10 ml of carbon tetrachloride was charged into a three-necked flask, fitted with mechanical stirrer, reflux condenser and dropping funnel. Then a mixture of 11 ml of sulfuric acid (d 1.84) and 3 ml of nitric acid (d 1.4) was added in 30 minutes to the reaction mass at 90-95° (sulfuric acid bath). The mixture was then heated another hour, 1.7 ml of nitric acid added in 15 minutes, and the synthesis terminated in 25 minutes. At reaction end the mixture was cooled and diluted with water. The unreacted iodine (0.3-0.5 g) was steam distilled, while the residue was filtered, washed with water, and recrystallized from glacial acetic acid. Yield of 4,4'-diiodobiphenyl 68% (13.9 g); m.p. 204°. The qualitative test for nitrogen was negative.

Found % I 62.35, 62.60. $C_{12}H_8I_2$. Calculated % I 62.51.

SUMMARY

4-Iodobiphenyl and 4,4'-diiodobiphenyl were obtained by the direct iodination of biphenyl in the presence of mixed acid.

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A NEW TYPE OF CATIONIC CATALYSIS

II. REACTION OF CARBOXYLIC ACIDS WITH PHOSPHORUS TRICHLORIDE

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As we had shown earlier, neutral salts (NaCl, KCl, etc.) are extremely active catalysts for some organic reactions. We discovered the catalytic effect of neutral salts in studying the reactions of phenols with $POCl_3$ [1,2]. Even those phenols (nitrophenols, picric acid) that ordinarily do not react with $POCl_3$ show rapid and facile reaction with $POCl_3$ in the presence of neutral salts. The fact that the reaction rate is dependent on the dissociation constant of the phenol made it possible to advance a theory for the mechanism of the catalytic effect of neutral salts, based on a rearrangement of the cation.

$$ArO^-H^+ + Na^+Cl^- \rightleftarrows ArONa + HCl \qquad (1)$$

$$ArONa + POCl_3 \rightarrow ArOPOCl_2 + NaCl \qquad (2)$$

It was postulated that the catalytic effect of neutral salts should also be manifested in some other reactions. Specifically, those reactions should be accelerated in which one component has a distinctly acid character, and the other component a fairly labile halogen atom. In addition, it is necessary to observe still two other conditions: 1) the hydrogen halide formed in the reaction should be poorly soluble in the reaction mixture, and 2) the reaction must be run at the boil to remove the hydrogen halide formed, as otherwise the equilibrium of reaction (1) will be shifted completely to the left and no catalytic effect will be observed. Actually, it was subsequently shown by us that the catalytic effect of neutral salts is also manifested in the reaction of carboxylic acids with thionyl chloride [3]. In complete harmony with the advanced mechanism it proved in this case also that the catalytic effect is manifested with especial clarity in the preparation of the chlorides of acids with a high dissociation constant, for example trichloroacetic acid, which, as is known, does not react with thionyl chloride [4,5]. In harmony with the above-indicated mechanism, the catalytic effect of neutral salts can occur only in the case where reaction proceeds with the intermediate formation of a mixed acid chloride.

$$RCOOH + SOCl_2 \rightarrow RCOOSOCl \rightarrow RCOCl \qquad (3)$$

The possibility of forming such a mixed acid chloride was also postulated earlier [4,7]. From the above it follows that the catalytic effect of neutral salts discovered by us has a general character and is applicable to a number of other reactions. In this paper we show that the catalytic effect of neutral salts is also observed in the reaction of carboxylic acids with phosphorus trichloride. It is interesting to mention that although this reaction has been known for a long time [6] and is frequently used to obtain carboxylic acid chlorides, still not a single opinion has been expressed up to now as to its mechanism. It is usually assumed that the reaction goes with the formation of $P(OH)_3$.

$$3RCOOH + PCl_3 \rightarrow 3RCOCl + P(OH)_3 \qquad (4)$$

Since the evolution of HCl is always actually observed, preference is frequently given to equation (5):

$$3RCOOH + 2PCl_3 \rightarrow 3RCOCl + P_2O_3 + 3HCl \qquad (5)$$

Lucas and Pressman [7] believe that the reaction proceeds according to scheme (6).

$$RCOOH + PCl_3 \rightarrow RCOOPCl_2 + HCl$$
$$\downarrow$$
$$RCOCl + POCl*$$

(6)

Cade and Gerrard [9] advance the following equation:

$$RCOOH + PCl_3 \rightarrow RCOCl + HOPCl_2.$$

(7)

Such an abundance of different opinions on the course of this reaction is explained by the fact that both the starting compounds and their reaction products are capable of reacting in a highly varied manner. For example, it is known that carboxylic acid chlorides react with phosphorous acid [10]; occasionally the formation of red phosphorus is observed, apparently due to the disproportionation of H_3PO_3 or of P_2O_3, etc. For this reason even a very detailed study of all of the possible reaction products and their proportions can hardly lead to an elucidation of the mechanism of this reaction. Of all of the equations given, only equation (6) permits the possibility of a catalytic acceleration of the reaction by neutral salts (similar to the reaction of phenols with $POCl_3$ and of carboxylic acids with $SOCl_2$ [1-3]). For this reason we assumed that a study of the possibility of utilizing the catalytic effect of neutral salts in the reaction of carboxylic acids with PCl_3 is of interest not only from the viewpoint of expanding the range in which the type of catalytic phenomena discovered by us can be utilized, but also from the standpoint of arriving at a decision as to the mechanism of this reaction.

The catalytic effect of neutral salts (KCl) in the reaction of carboxylic acids with PCl_3 was studied by us on a number of examples. We judged as to the kinetics of the reaction by the rate of HCl evolution (using the earlier-described method [1-3]). It proved in all cases, independent of whether a neutral salt was or was not added, that 1 mole of HCl was always evolved per mole of acid taken (even when a large excess of PCl_3 was taken). The kinetics for the reactions of CCl_3COOH and $CH_2ClCOOH$ with PCl_3 are given in the graph. Since in the case of these reactions, in contrast to that described by us earlier [2], the process goes at a measurable speed even in the absence of a neutral salt, it proved possible to calculate the increase in the rate constant for the reaction. For this we utilized the fact that the ratio k'/k is inversely proportional to the ratio t'/t, where t and t' are respectively equal to the reaction time. Actually, $k = \frac{1}{t} \ln \frac{a}{a-x}$ (A)

Kinetics of reaction of carboxylic acids with PCl_3
1) CCl_3COOH, 2) $CH_2ClCOOH$, 1k—CCl_3COOH (in the presence of KCl), 2k—$CH_2ClCOOH$ (in the presence of KCl).

and $k' = \frac{1}{t'} \ln \frac{a'}{a'-x}$ (B).

If $a = a'$ and $x = x'$, then after dividing (A) by (B) we obtain: $k:k' = t':t$. From the given curves it can be seen that monochloroacetic acid (dissociation constant $k = 1.5 \cdot 10^{-3}$) reacts quite rapidly with PCl_3 even without a catalyst (Curve 2) and to the extent of 50% in 45 minutes, while in the presence of KCl it reacts to the extent of 50% in 11 minutes (Curve 2k), i.e. the rate constant shows a 4-fold increase. Trichloroacetic acid ($k = 2 \cdot 10^{-1}$) reacts to the extent of 20% in 85 minutes without catalyst, and to the same extent in 6 minutes in the presence of KCl, i.e. the rate constant for the reaction shows a 14-fold increase. The reaction of PCl_3 with α-bromopropionic and α-bromoisovaleric acids also increases in exactly the same manner in the presence of KCl: in these cases the reaction-rate constant shows only a 2-fold increase, since these acids have lower dissociation constants ($1.0 \cdot 10^{-5}$). Consequently, also in the reaction of carboxylic acids with phosphorus trichloride the addition of a small amount of neutral salt catalytically accelerates the reaction, and completely analogous to our earlier-described examples, the degree of acceleration is largely dependent on the dissociation constant of the taken acid. Practically, the addition of a neutral salt does not play a major role in the preparation of the chlorides of carboxylic acids with a low dissociation constant, since these acids react quite vigorously with PCl_3

*See the paper by Besson [8].

and $SOCl_2$ even in the absence of a neutral salt. However, the situation changes sharply when the matter is one of obtaining the chlorides of strongly dissociated acids (trichloroacetic acid, dichloroacetic acid, etc.), since in general these acids either do not react with $SOCl_2$ and PCl_3 or react very slowly in the absence of a neutral salt. In these cases the addition of a neutral salt proves to be highly beneficial, and the reaction proceeds rapidly and with a good yield of acid chloride. However, a lower yield of chloride is obtained when carboxylic acids are reacted with PCl_3 than when $SOCl_2$ is used (this is independent of whether a neutral salt is added or not). A possible explanation for this is the fact that it is difficult to effect a complete removal of acid chloride from the obtained hard residue by distillation.

EXPERIMENTAL

Kinetics of the reaction of carboxylic acids with PCl_3. A charge of 0.05 g-mole of carboxylic acid and 0.2 g-mole of PCl_3 was placed in a round-bottomed flask fitted with a ground-glass reflux bulb condenser, and the mixture heated at the boil during the whole experiment. The evolved hydrogen chloride passed through a tube filled with pieces of unglazed porcelain, moistened with sulfuric acid, and then was absorbed in an accurately measured amount of 1N NaOH. The NaOH solution was replaced by new solution at periodic intervals, and the amount of evolved hydrogen chloride was determined. The kinetics of the reaction in the presence of KCl (always 0.1 g of KCl was added) was determined the same way. The obtained data are plotted in the graph.

The carboxylic acid chlorides were prepared in conventional manner. One gram of KCl was added to 1 g mole of taken acid. The reaction solution was heated on the water bath until HCl ceased to evolve. After removal of excess PCl_3 the acid chlorides were isolated by distillation under a moderate vacuum (150-240 mm) to avoid losses. Then the acid chlorides were redistilled at atmospheric pressure through a column. The following chlorides were isolated:

1) monochloroacetyl chloride (yield 62%, b.p. 103-104.5°);

2) α-bromopropionyl chloride (yield 61%, b.p. 125-129°);

3) trichloroacetyl chloride (yield 70%, b.p. 115-116°).

SUMMARY

1. It was shown that the reaction of carboxylic acids with phosphorus trichloride is accelerated in the presence of neutral salts (KCl). The acceleration depends to a large degree on the dissociation constant of the acid. The greatest acceleration is observed in the case of strong acids. In the case of trichloroacetic acid the reaction-rate constant shows a 14-fold increase, and in the case of monochloroacetic acid only a 4-fold increase.

2. The opinion was expressed that the ability of neutral salts to catalytically accelerate the reaction of carboxylic acids with PCl_3 supports the mechanism proposed by Lucas and Pressman for the reaction.

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A NEW TYPE OF CATIONIC CATALYSIS

III. REACTION OF CARBOXYLIC ACID CHLORIDES WITH ACIDS AND PHENOLS

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The catalytic effect of neutral salts (NaCl, KCl, etc.) in some organic reactions was described in earlier communications [1-4]. An investigation of the following two reactions is described in this communication.

$$RCOOH + RCOCl \rightarrow (RCO)_2O + HCl$$

$$ArOH + RCOCl \rightarrow ArOCOR + HCl$$

Both reactions satisfy the conditions under which it is possible for the catalytic activity of neutral salts to be manifested [1]: one component has an acid character (it can take part in the rearrangement of the cation), and the second component has a labile halogen atom. The first reaction not only makes it possible to expand the utility of the new type of cationic catalysis discovered by us, but it also serves as a method of obtaining acid anhydrides.

Of the large number of different methods available for obtaining carboxylic acid anhydrides the following two methods are usually recommended [5]: the exchange reaction of a carboxylic acid with some readily available anhydride, and the reaction of an acid chloride with an acid in the presence of an equimolar amount of pyridine. In the case of the second reaction the hygroscopic precipitate of pyridine hydrochloride is filtered and washed with benzene, while the acid anhydride is isolated from the filtrate by distillation in a yield of 78 to 83% The possibility of obtaining acid anhydrides by the direct reaction of carboxylic acids with their acid chlorides has been neglected. The first data on obtaining an acid anhydride by heating an acid with its chloride are given by Linnemann and Zotta [6], who obtained butyric anhydride in 86% yield by heating a mixture of butyric acid and butyryl chloride. J. Kanonnikoff and M. Saytzeff [7] obtained acetic anhydride in 50% yield by heating a mixture of

Fig. 1. Kinetics of the reaction of carboxylic acids with their chlorides.
1) $CCl_3COOH + CCl_3COCl$,
2) $CH_2ClCOOH + CH_2ClCOCl$,
3) $n - C_3H_7COOH + C_3H_7COCl$.
The lettered curves represent those obtained when the reaction was run in the presence of KCl.

acetyl chloride with glacial acetic acid. Later this method of preparing acetic anhydride was even patented [8], and quite recently a patent was granted for the preparation of benzoic anhydride by a similar method [9]. Apparently, the unpopularity of this method for obtaining acid anhydrides was evoked by the paper of R. Anschutz [10], who, investigating various methods of obtaining acid anhydrides, came to the conclusion that the reaction of carboxylic acids with their chlorides "proceeds slowly and incompletely".

The catalytic effect of neutral salts in the reaction of carboxylic acids with their chlorides was studied by us on a number of examples. The same as before, we judged as to the kinetics of the reaction by the rate of HCl evolution, using the earlier-described method [1,2]. The data obtained by us are plotted in Fig. 1. From the given
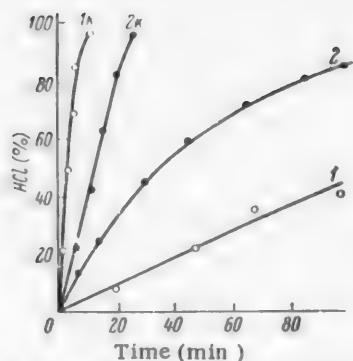
Fig. 2. Kinetics of the reaction of
carboxylic acid chlorides with phenols.
1) $(O_2N)_2C_6H_3OH + CH_2ClCOCl$,
2) $(O_2N)_2C_6H_3OH + C_3H_7COCl$.
The lettered curves represent those
obtained when the reaction was run
in the presence of $(CH_3)_4NCl$,

curves it can be seen that the greatest acceleration of the reaction from the addition of KCl is observed in the case of reaction using trichloroacetic acid: without catalyst the reaction goes to the extent of 50% in 64 minutes, while in the presence of KCl the reaction goes to the same extent in 11 minutes, i.e. the reaction rate constant shows a 6-fold increase [4]. In the case of monochloroacetic acid the reaction rate constant shows a 3-fold increase, and in the case of the even less dissociated acids—butyric and benzoic — it shows an increase of 1.6 and 2 times. As a result, our earlier-found rule [1-4] is also applicable to the reaction of carboxylic acids with their chlorides; in this case also the catalytic effect of neutral salts   depends to a large degree on the dissociation constant of one of the reaction components (CCl_3COOH had $k = 2 \cdot 10^{-1}$, $CH_2ClCOOH$ has $k = 1.5 \cdot 10^{-3}$, and $n-C_3H_7COOH$ has $k = 1.6 \cdot 10^{-5}$).

Our experiments also revealed that acid anhydrides are obtained in very good yield using this reaction; for example, trichloroacetic anhydride was obtained in 82.8% yield, butyric anhydride in 87.5% yield, and monochloroacetic anhydride in 70% yield. If a large excess of the acid chloride is used, then the yield of anhydride is increased even more. Thus, for example, using a 100% excess of CCl_3COCl, the anhydride of trichloroacetic acid was obtained in 95% yield. The results obtained by us permit recommending this method of synthesizing acid anhydrides in all those cases where neither the acid chloride nor the acid anhydride is decomposed when boiled.

Since both the reaction of carboxylic acids with thionyl chloride and the reaction of carboxylic acids with their chlorides are accelerated in the presence of neutral salts, there is no need for starting with the acid chlorides to obtain acid anhydrides: the same results can be achieved by reacting the carboxylic acid (2 moles) with thionyl chloride (1 mole). We hope to publish soon on the catalysis of this reaction with neutral salts and on the results obtained.

The acylation of phenols seemed of interest to us as a further expansion of the possible application of cationic catalysis, and also from the viewpoint of confirming the validity of the hypothesis proposed by us for the mechanism of this type of catalysis. Actually, if the catalytic effect of a neutral salt is achieved through rearrangement of the cation [1,2]

$$RCOO^-H^+ + Na^+Cl^- \rightleftarrows RCOONa + HCl,$$

then the effectiveness of the catalytic effect of a neutral salt will depend to a large degree on the ionizing ability of the solvent, i.e. on the dielectric constant of the component that is taken in excess (acid chloride). Consequently, it could be expected that using an acid chloride with a high dielectric constant will result in a greater acceleration of the reaction rate.

The applicability of cationic catalysis in the acylation of phenols was checked by us on the examples of reacting 2,4-dinitrophenol with chloroacetyl chloride and butyryl chloride. 2,4-Dinitrophenol was chosen for the reason that the catalytic effect of a neutral salt is manifested most clearly here — the indicated dinitrophenol has a high dissociation constant ($k = 1.1 \cdot 10^{-4}$), which, as is known [1,2], exerts a large influence on the effectiveness of the catalytic effect of a neutral salt. The mentioned acid chlorides were chosen on the basis that they have close boiling points (108 and 102°) and differ sharply in the value of their dielectric constant. The method of operation was the same as that used earlier. As catalyst in these experiments we used $(CH_3)_4NCl$, since such salts as NaCl and KCl are completely insoluble in acid chlorides and naturally could not manifest a catalytic activity. The obtained results are plotted in Fig. 2, from which it can be seen that chloroacetyl chloride reacts quite sluggishly with the dinitrophenol — it takes 100 minutes for the reaction to go 40%. When the reaction is run in the presence of $(CH_3)_4NCl$ the same degree of reaction (40%) is obtained in 3 minutes. The addition of the neutral salt caused the reaction-rate constant to increase approximately 30 times. The reaction

of butyryl chloride without catalyst was somewhat more rapid — the reaction went to the extent of 40% in 25 minutes, while in the presence of $(CH_3)_4NCl$ it went to the same extent in 10 minutes. In this case the increase in the rate constant was only 2.5 times. This example shows the large role played by the ionizing ability of the acid chloride in cationic catalysis. After distilling off the excess chloride the corresponding 2,4-dinitrophenol esters were isolated from the residue. Consequently, on the basis of our studies [1-4] it can be said that the catalytic effect of neutral salts discovered by us bears a general character and is manifested in all those reactions where one component has an acid character and the second contains a labile halogen atom. To show the catalytic activity of a neutral salt it is necessary to run the reaction at the boil. The sharp dependence of the effectiveness of adding a neutral salt on the dissociation constant of the acid component and on the dielectric constant of the second component is extremely convincing evidence that the mechanism of the catalytic effect of a neutral salts is based on ionic reactions and that the scheme proposed by us for the catalytic effect of neutral salts[1],for example

$$ArO^-H^+ + Na^+Cl^- \rightleftarrows ArONa + HCl$$

$$ArONa + POCl_3 \rightarrow ArOPOCl_2 + NaCl,$$
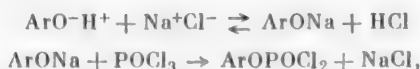
is probable and does not stand in contradiction to the experimental data, making it possible to correctly predict results.

It is interesting to discuss from the viewpoint of the catalytic phenomena discovered by us, the question of using the metal salts $ZnCl_2$, $AlCl_3$ and $FeCl_3$ in some reactions. The running of reactions in the presence of the indicated salts is frequently described in studies of a preparative nature. In not all cases can the mechanism of the action of these salts be explained from the viewpoint of cationic catalysis (for example, the Friedel-Crafts reaction), but in some cases there can hardly be any doubt but that the use of $AlCl_3$, for example, is due to the catalytic activity of the cation and that $AlCl_3$ can be successfully replaced by other salts. We will give an example of this. In 1884 Pawlewski [11] found that the reaction

$$C_6H_5OH + ClCOOC_2H_5 \rightarrow C_6H_5OCOOC_2H_5 + HCl$$

proceeds well in the presence of anhydrous aluminum chloride. There can hardly be any doubt but that the Pawlewski reaction is only a particular case of cationic catalysis. Actually, all of the conditions making it possible for the catalytic activity of the cation to be manifested are present in this reaction: one component has an acid character, and the second component has a labile halogen atom and a quite high dielectric constant ($\epsilon = 10.0$). In these respects the Pawlewski reaction is completely analogous to the reaction of C_6H_5OH with $POCl_3$, which, as has been shown by us, is accelerated in the presence of nearly any salt. There is no question but that also in the Pawlewski reaction it is possible to use other cations as catalysts (apparently, the most effective will be the salts of organic bases; see above). There can also be no doubt of the fact that the addition of a neutral salt will be even more effective when the Pawlewski reaction is run with nitrophenols. Obviously, it is possible to find still other reactions where the addition of $ZnCl_2$, $AlCl_3$ and $FeCl_3$ can be explained from the viewpoint of cationic catalysis.

EXPERIMENTAL

Preparation of Carboxylic Acid Anhydrides. Study of the Rate of Reaction of Trichloroacetic Acid with Its Own Acid Chloride

The rate of this reaction, both with and without catalyst, was determined by the earlier-described method [1,2]: a solution of 0.1 g-mole of the acid in 0.125 g-mole of the acid chloride, containing 0.15 g (0.002 g-mole) of KCl, was boiled in a round-bottomed flask fitted with a ground-glass reflux condenser. The evolved HCl was trapped in an exactly measured amount of 1N NaOH, which was periodically replaced by a new solution, and titrated with 1N NaOH. The results of measuring the amount of HCl evolved are given in the table.

Using the same method we determined the reaction rate for the preparation of other anhydrides, and the results of these measurements are plotted in Fig. 1.

Preparation of $(CCl_3CO)_2O$ (I). A mixture of 32.7 g of CCl_3COOH, 41.9 g of CCl_3COCl and 0.3 g of KCl was heated under reflux for 2 hours. The obtained anhydride was carefully decanted from the potassium chloride and then fractionally distilled in vacuo; we obtained 51.2 g (82.8%) of (I) with b.p. 130-134° at 47 mm.

Reaction time (in minutes)	1N NaOH consumed in titration of evolved HCl (ml)		Amount of HCl evolved (in % of the theoretical)	
	without catalyst	with KCl	without catalyst	with KCl
4	—	22.3	—	22.3
7	9.3	—	—	46.6
9	—	24.3	—	46.6
14	10.6	—	19.9	—
20	—	22.4	—	69.0
25	9.9	—	29.8	—
30	—	10.7	—	79.7
40	9.4	—	39.2	—
45	—	9.0	—	88.7
60	—	4.0	—	92.7
62	10.0	—	49.2	—
87	7.4	—	56.6	—
90	—	3.0	—	95.7
117	7.1	—	63.7	—
165	10.9	—	74.6	—
240	9.6	—	84.2	—
300	5.5	—	89.2	—
360	3.7	—	93.4	—

Preparation of (I) using a large excess of CCl_3COCl. A mixture of 32.7 g of CCl_3COOH, 73.0 g of CCl_3COCl and 0.3 g of KCl was refluxed for 2 hours. Then the liquid was decanted from the KCl and rectified in vacuo. After distilling off the excess CCl_3COCl (31.4 g) we obtained 59.3 g (95.7%) of (I) with b.p. 139-141° at 60 mm.

Preparation of $(CH_2ClCO)_2O$ (II). A mixture of 18.8 g of $CH_2ClCOOH$, 26.0 g of $CH_2ClCOCl$ and 0.3 g of KCl was refluxed for 2 hours, the liquid decanted from the KCl, and the product vacuum distilled. We obtained 28 g of product with b.p. 115-125° at 16 mm; redistillation gave 23 g (67%) of the anhydride with b.p. 120-123° at 20 mm.

Preparation of $(n-C_3H_7CO)_2O$ (III). A mixture of 35.2 g of $n-C_3H_7COOH$, 85.2 g of $n-C_3H_7COCl$ and 0.6 g of KCl was refluxed for 1.5 hours; the liquid after cooling was decanted from the KCl and rectified in vacuo. We obtained 36.2 g of unreacted acid chloride with b.p. 106-112° and 55.3 g of (III) with b.p. 108-110° (37 mm); yield 87.5%.

Acylation of 2,4-Dinitrophenol

1. Reaction of 2,4-dinitrophenol with monochloroacetyl chloride. A mixture of 9.4 g of 2,4-dinitrophenol, 45.2 g (0.4 mole) of $CH_2ClCOCl$ and 0.12 g of $(CH_3)_4NCl$ was refluxed. The evolved HCl was trapped in 1N NaOH (using the above-described method). The results of measuring the amount of HCl evolved are plotted in Fig. 2 (Curve 1k). On conclusion of reaction (30 minutes) the excess acid chloride was removed by vacuum distillation; the residue — 2,4-dinitrophenyl monochloroacetate — crystallized. Yield 13.4 g (quantitative); m.p. 97-98° (from chloroform).

Found % N 10.70. $C_8H_5O_6N_2Cl$. Calculated % N 10.75.

The kinetics of the reaction in the absence of $(CH_3)_4NCl$ was determined in a similar manner (Curve 1, Fig. 2).

2. Reaction of 2,4-dinitrophenol with n-butyryl chloride. A mixture of 9.4 g of 2,4-dinitrophenol, 42.7 g of n-butyryl chloride and 0.12 g of $(CH_3)_4NCl$ was refluxed. The evolved HCl was trapped in 1N NaOH, as described above. The results of measuring the amount of HCl evolved are shown in Fig. 2, Curve 2k. After distilling off the excess butyryl chloride we obtained 12.6 g of 2,4-dinitrophenyl butyrate. The ester was obtained as a light-yellow liquid; small portions can be vacuum distilled; b.p. 170-172° (2 mm).

Found % N 10.77. $C_{10}H_{10}O_6N_2$. Calculated % N 11.02.

SUMMARY

1. The reaction of carboxylic acids with their chlorides is accelerated substantially in the presence of neutral salts. In the case of the more highly dissociated acids this increase in the reaction rate is quite great. The fact that this method gives good yields of acid anhydrides permits recommending it for their preparation.

2. The reaction of 2,4-dinitrophenol with carboxylic acid chlorides is also accelerated substantially in the presence of neutral salts.

3. The dependence of the accelerating effect shown by neutral salts on the dielectric constant of the carboxylic acid chloride indicates that the catalytic effect has an ionic mechanism and supports the theory expressed earlier regarding the mechanism of cationic catalysis.

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CYCLOSERINE AND RELATED COMPOUNDS

IV. α-BENZAMIDOACRYLHYDROXAMIC ACIDS

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In connection with studies being made in our laboratory [1-3] on the synthesis of the recently discovered antibiotic cycloserine and of compounds related to it, we deemed it expedient to include some hydroxamic acids, having an acylamino group in the α-position, in our study. Further study of some of the transformations of these compounds could open a new route to the synthesis of cycloserine analogs. The present paper is devoted to the synthesis of β-substituted α-benzamidoacrylhydroxamic acids.

The reaction of azlactones with hydroxylamine could serve as the most convenient way of synthesizing these compounds. This reaction was run on the simplest example, 2-phenyl-4-benzylidene-oxazolone (Ia), by Shaw and McDowell [4], who effected cleavage of the azlactone by treatment with free hydroxylamine in anhydrous methanol. The reaction proved to be ill-defined under these conditions, as a result of which the yield of α-benzamido-β-phenylacrylhydroxamic acid (IIa) did not exceed 50%; together with this another compound was isolated in 25% yield, which compound was assigned the structure of α-benzamido-β-phenyl-β-hydroxyamino-propionic acid by the authors [5].

We made a detailed study of the reaction of azlactones with hydroxylamine under various conditions. It proved that the pH of the medium exerts a very large influence on the reaction results, in which connection the optimum pH is 5-6.5. At a higher pH the reaction proves to be ill-defined and is complicated by the addition of hydroxylamine to the double bond (which also occurred in the case described by Shaw and McDowell), the formation of esters of α-benzamidocinnamic acid, etc. At a lower pH the reaction proves to be slightly too slow (see [6]), although in case of need, by increasing the reaction time, it is possible to obtain good yields even at a pH of 4. In practice it is most convenient to effect cleavage of the azlactone using a methanol solution of hydroxylamine acetate at 10-50°; operating at a higher temperature leads to further transformations of the reaction products.

For methanol-soluble azlactones the cleavage with hydroxylamine proceeds to the extent of 92-96% at 20° in 45-55 minutes, and only in the case of difficultly soluble compounds does it prove necessary to increase the reaction time or raise the temperature.

The method worked out by us for the synthesis of β-substituted derivatives of α-benzamidoacrylhydroxamic acids proved to be general, and suitable for obtaining acids with different substitutents in the aromatic ring (methoxy, methylenedioxy, nitro, dimethylamino and halogen). The acids were easily obtained from the corresponding readily available azlactones in yields exceeding 80%.

The nature of the substitutent apparently exerts very little influence on the yield, and only in the case where (II) is noticeably soluble in aqueous methanol does the yield drop due to incomplete separation, whereas photocolorimetric determination reveals that 92-96% of the azlactone has been converted. This method is evidently also suitable for obtaining various derivatives containing a heterocyclic radical; we used the method to synthesize the β-(α-furyl)-substituted compound (IIe). Finally, it is apparently also quite suitable for obtaining α-benzamidoacrylhydroxamic acis with aliphatic radicals in the β-position. Thus, when 2-phenyl-4-

isopropylideneoxazolone (Ih) was reacted under the above-described conditions we isolated α-benzamido-β,β-dimethylacrylhydroxamic acid (IIh) in about 60% yield.
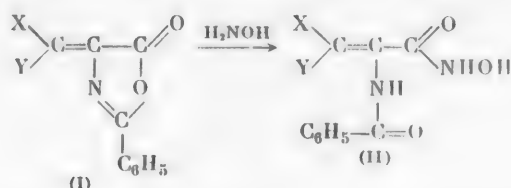
Compound	X	Y	Compound	X	Y
Ia, IIa	C_6H_5	H	Ie IIe		H
Ib, IIb	p-$CH_3OC_6H_4$	H	If IIf	p(CH_3)$_2$N—C_6H_4	H
Ic, IIc	3,4-$CH_2O_2C_6H_3$	H	Ig IIg	p-BrC_6H_4	H
Id, IId	m-$O_2NC_6H_4$	H	Ih IIh	CH_3	CH_3
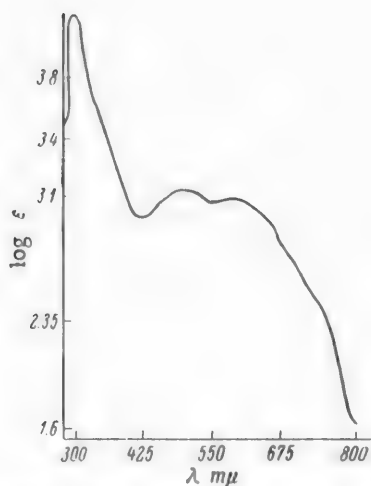
Absorption spectrum of the complex of α-benzamido-β-(3,4-methylenedioxy-phenyl)acrylhydroxamic acid (C = 10^{-3}) with $FeCl_3$.

As is well known [5], hydroxamic acids are extremely unstable at elevated temperatures. For this reason we use a much milder isolation method than that described in [4], reducing to a throwing-out of the hydroxamic acid from methanol solution with water, followed by a careful precipitation of the substance from dilute alkaline solution with acid in the presence of a small amount of ethyl acetate. The β-substituted α-benzamidoacrylhydroxamic acids obtained in this manner, based on the elementary analysis data and the spectral characteristics, proved to be quite pure. They represent crystalline compounds, are readily soluble in aqueous alkali solutions, and are precipitated on acidification of the alkaline solution. They are easily changed if heated or if subjected to a prolonged or more drastic exposure to the action of acids or alkalies.

The α-benzamidoacrylhydroxamic acids give characteristic green-colored copper salts. Their complexes with ferric salts show a characteristic absorption spectrum in the visible region, which is independent of the substituent in the β-position and is identical for all of the members obtained by us in this series (figure).

When the aqueous alkaline solutions of the obtained β-substituted α-benzamidoacrylhydroxamic acids were acidified to different pH values we observed that the melting points of the resulting precipitates changed, and at times this change was quite substantial.• In exactly the same manner, running the reaction of azlactones with hydroxylamine at different temperatures leads to obtaining hydroxamic acids that have somewhat different melting points. For example, when (IIa) is obtained under conventional conditions (see below) its m.p. is 106-107°, while if the reaction is run at 40-45° the obtained compound (IIa) has m.p. 128-130°. This phenomenon is most probably associated with a change in the geometric configuration of the hydroxamic acid, although other reasons are not excluded. Similar results were also observed for some glyoxalidones and oxazolones [7-10]; we are currently studying this problem in greater detail.

• It should be mentioned that in general the melting point is not a sufficient characteristic for hydroxamic acids, since the latter do not have a sharp melting point, but instead show vigorous decomposition in a narrow temperature range.

The β-substituted α-benzamidoacrylhydroxamic acids obtained by us were subjected to catalytic hydrogenation. It proved that under mild conditions these compounds smoothly absorb 1 mole of hydrogen and are converted to the corresponding α-benzoyl-β-arylalanylhydroxamic acids, which are new. The method described here is a very convenient way of preparing them. In this connection it is interesting to mention that the different specimens of the same β-substituted α-benzamidoacrylhydroxamic acid, differing in melting point because of reprecipitation at different pH values (see above), all give a β-aryl-α-benzoylalanylhydroxamic acid with completely identical properties.

The obtained substituted α-benzamidohydroxamic acids under mild hydrolysis give known α-benzoyl-β-arylalanines, and when treated with 10% hydrochloric acid and methanol they give the corresponding esters. For a number of the members described in this paper we prepared the last two types of compounds both for the purpose of identification and in connection with their antibacterial action (for example, α-benzamidocinnamic acid inhibits the growth of both gram-positive and gram-negative bacteria in concentrations of 30 γ /ml). They were synthesized in conventional manner, i.e. by treating the azlactones with aqueous-alcoholic caustic to obtain the acids [10], or with methanol in the presence of catalytic amounts of alkali to obtain the esters [10,11].

The β-substituted α-benzamidoacrylic acids and their esters obtained in this manner were easily converted to α-benzoyl-β-arylalanine derivatives by catalytic hydrogenation over palladium on barium sulfate, which can possess independent interest as a method of synthesizing α-benzoyl-β-arylalanines.

The earlier-known reduction methods-hydrogenation over platinum at 3 atm [12], over nickel at 50-100 atm [13], and reduction with hydriodic acid [12] or with sodium amalgam [14] — are less convenient and give poorer yields.

The discussed transformations can be depicted by the following general scheme.
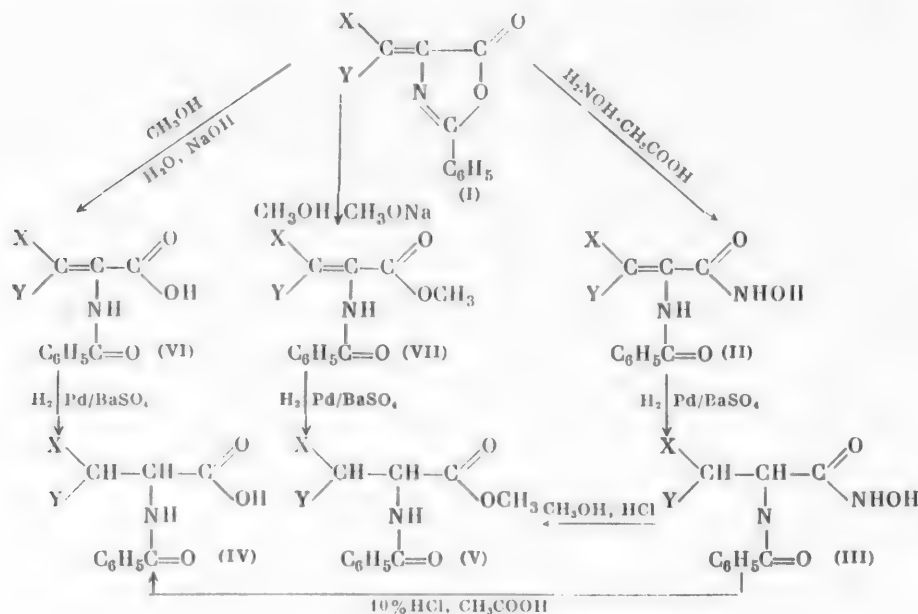
This cycle of transformations fully proves the structure of the α-benzoyl-β-arylalanylhydroxamic acids obtained by us and of the α-benzamido-β-arylacrylhydroxamic acids serving as starting substances for their preparation, and consequently also clearly demonstrates the course of the reaction of azlactones with hydroxylamine investigated by us.

Testing of the obtained β-aryl-α-benzamidoacrylhydroxamic acids, done by M. A. Breger in the Chemotherapy Section of our Institute, revealed that some of the compounds in this series possess definite in vitro bacteriostatic activity and in concentrations of 50-100 γ /ml inhibit the growth of both gram-negative and gram-positive bacteria. Of the obtained compounds the most active are (IId), (IIf) and (IIg).

Preparation of a 0.57N methanol solution of hydroxylamine acetate. For this, equal volumes of an 8% methanol solution of hydroxylamine hydrochloride and a 12% methanol solution of potassium acetate were mixed and the potassium chloride removed by filtration.

α-Benzamido-β-arylacrylhydroxamic acids. A mixture of 0.03 g-mole of 2-phenyl-4-arylideneoxazolone and 200 ml of the above methanol solution of hydroxylamine acetate was stirred for some time. In the case where the hydroxamic acid precipitated, it was filtered and the filtrate was diluted with cold water, which precipitated additional compound. If the acid did not precipitate, then the dilution with water was made immediately after reaction was ended and the hole allowed to stand overnight at -10°. The hydroxamic acid was next dissolved with cooling in 5% sodium hydroxide solution, the solution extracted with ethyl acetate, then acidified carefully to pH 1-2, the precipitate filtered, then washed with water and ethyl acetate, and dried. With such purification the melting point of the hydroxamic acid went up only in those cases where the starting compounds were insufficiently pure or where the reaction time had been decreased to the point where reaction was incomplete. The data on the reaction conditions and the yields and constants of the obtained α-benzamido-β-arylacrylhydroxamic acids are summarized in Table 1.

The obtained hydroxamic acids form characteristic dark-green copper salts, from which they can be quantitatively regenerated by decomposition with 10% sulfuric acid in the cold, and they give an intense color with ferric chloride solution, having a characteristic absorption spectrum (figure). On long standing some of the specimens suffer gradual decomposition with the evolution of nitrogen oxides.

TABLE 1

Synthesis of α-Benzamido-β-arylacrylhydroxamic Acids   ArCH=CCONHOH
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad |$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad NHCOC_6H_5$$
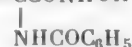
Ar	Reaction conditions time (in hours)	temp. of melting decomp.)	Yield (in %)	Melting point (decomp.)	Amount (in %) C found	C calc.	H found	H calc.	N found	N calc.
C_6H_5	1	18—20°	87—94	106—107°	—	—	—	—	9.93	9.92 •
p-$CH_3OC_6H_4$	12	18—20	82	106—107	—	—	—	—	8.80	8.96
3,4-$CH_2O_2C_6H_4$	0.5—0.75	45—50	83	91—93	62.87	62.57	4.42	4.29	8.38	8.58
m-$NO_2C_6H_4$	1	18—20	70	110—112	58.42	58.66	4.29	4.00	13.20	13.14
p-$(CH_3)_2NC_6H_4$	0.5—0.75	45—50	90	112—113	66.47	66.44	5.95	5.90	12.93	12.90
p-BrC_6H_4 • •	12	18—20	100	114—115	—	—	—	—	—	—
α-Furyl	1	18—20	70	119—120	61.90	61.75	4.53	4.44	10.22	10.28

•Literature [4]: m.p. 128-130°.

• •Found % Br 22.10; calc. 22.12.

α-Benzamido-β,β-dimethylacrylhydroxamic acid. Obtained in the same manner as above from 4.3 g of 2-phenyl-4-isopropylideneoxazolone and 100 ml of the above-described methanol solution of hydroxylamine acetate. The clear solution was evaporated in vacuo to a sirup, extracted with ethyl acetate, and the hydroxamic acid precipitated from the extract by the addition of petroleum ether. Colorless crystals; m.p. 134-136°; yield 3.0 g (61%).

Found % C 61.65; H 6.13. $C_{12}H_{14}O_3N_2$. Calculated % C 61.53; H 6.00.

α-Benzamido-β-arylalanylhydroxamic acids. A solution of 0.03 g-mole of the α-benzamido-β-aryl-acrylhydroxamic acid in 150 ml of methanol was hydrogenated at room temperature and atmospheric pressure using 5% palladium on barium sulfate. After 1 mole equivalent of hydrogen had been absorbed the catalyst was filtered, the filtrate evaporated in vacuo at 30° to a volume of 30-50 ml, and the residue diluted with 150 ml of

water and allowed to stand overnight at -10°. The precipitate was filtered and then recrystallized from alcohol. The data on the α-benzoyl-β-arylalanylhydroxamic acids obtained in this manner are summarized in Table 2. The α-benzoyl-β-arylalanylhydroxamic acids give a crimson color with ferric chloride.

TABLE 2

Synthesis of α-Benzoyl-β-arylalanylhydroxamic Acids $ArCH_2CHCONHOH$

$NHCOC_6H_5$

Ar	Yield (in %)	Melting point	N Content (in %)	
			found	calculated
C_6H_5	80	143—144°	10.00	9.85
p-$CH_3OC_6H_4$	70	148—149	8.92	8.90
3,4-$CH_2O_2C_6H_3$	70	151—152	8.23	8.54
p-$(CH_3)_2NC_6H_4$ •	64	167—168	C 66.44	66.03
			H 6.75	6.47

• This compound contains NCH_3 groups, for which reason the nitrogen determination does not give good results.

The α-benzoyl-β-phenylalanylhydroxamic acid. a) A suspension of 5.4 g of α-benzoyl-β-phenyl-alanylhydroxamic acid in a mixture of 150 ml of 10% hydrochloric acid and 75 ml of methanol was refluxed for 1.5 hours (until the test with ferric chloride was negative), after which the methanol was vacuum distilled, the residue made alkaline with 5% caustic, then extracted with ether and the water layer acidified; we obtained 1.9 g (37%) of colorless crystals with m.p. 178-180°. The mixed melting point with an authentic specimen of α-benzoyl-phenylalanine was not depressed. Literature [15]: m.p. 180-182°.

The ether extracts were evaporated to give 2.8 g (52%) of substance; after recrystallization from alcohol, m.p. 84-85°. The mixed melting point with an authentic specimen of the methyl ester of α-benzoyl-β-phenyl-alalanine was not depressed. Literature [16]: m.p. 86-87°.

b) A solution of 4 g of α-benzoyl-β-phenylalanylhydroxamic acid in a mixture of 40 ml of glacial acetic acid and 40 ml of 10% hydrochloric acid was refluxed for 30 minutes and then cooled: we obtained 2.3 g (62%) of α-benzoyl-β-phenylalanine; m.p. 178-180° (from alcohol).

Hydrolysis of the other α-benzoyl-β-arylalanylhydroxamic acids in a similar manner gave: α-benzoyl-β-(p-methoxyphenyl)-alanine (IVb) (yield 95%; m.p. 162-164°); and α-benzoyl-β-(3,4-methylenedioxyphenyl) alanine (IVc) (yield 83%; m.p. 168-170°).

Synthesis of α-benzamidocinnamic acids. A solution of 0.03 g-mole of 2-phenyl-4-arylideneoxazolone in 150 ml of a 2% sodium hydroxide solution in 50% methanol was refluxed for 30 minutes, then cooled, acidified to pH 5-5.5, and the precipitate filtered, and washed with water and then with ether. Dilution of the mother liquor with water gave a second yield of the compound. Both yields proved to be quite pure and did not require further purification. Using the same method we obtained α-benzamidocinnamic acid (VIa) (yield 92%; m.p. 228-230°, from alcohol), α-benzamido-p-methoxycinnamic acid (VIb) (yield 82%; m.p. 220-222°,from alcohol), α-benzamido-3,4-methylenedioxycinnamic acid (VIc) (yield quantitative; m.p. 228-229°, from aqueous dioxane) and α-benzamido-p-dimethylaminocinnamic acid (VIf) (yield quantitative; m.p. 212-213°, from alcohol).

Found %: C 70.06; H 6.04; N 9.11. $C_{18}H_{18}O_3N_2$. Calculated %: C 69.99; H 5.86.

Synthesis of α-benzoyl-β-arylalanines. The α-benzamidocinnamic acids were hydrogenated in methanol over 5% palladium on barium sulfate at room temperature and atmospheric pressure. Using this procedure we obtained (IVa), (IVb), (IVc) and (IVf) in quantitative yields (see above for the constants).

Synthesis of methyl esters of α-benzamidocinnamic acids. A suspension of 0.03 g-mole of 2-phenyl-4-arylideneoxazolone in 100 ml of methanol, containing 0.1 g of sodium hydroxide, was stirred at room temperature for 2 hours. The color of the precipitate changed. The precipitate was filtered and washed with methanol; dilution of the methanol mother liquors with water gave an additional amount of the substance. Using this procedure we obtained methyl α-benzamidocinnamate (VIIa) (yield 93%; m.p. 139-141°, from methanol), methyl α-benzamido-p-methoxycinnamate (VIIb) (yield 92%; m.p. 141-142°, from methanol), methyl α-benzamido-3,4-methylenedioxycinnamate (yield quantitative; m.p. 130-132°, from methanol) and methyl α-benzamido-p-dimethylaminocinnamate (VIIf) (yield 96%; m.p. 171-173°, from methanol).

Synthesis of methyl ester of α-benzoyl-β-arylalanines. The methyl esters of the α-benzamidocinnamic acids were hydrogenated in methanol over 5% palladium on barium sulfate at room temperature and atmospheric pressure. With this procedure we obtained the methyl esters of α-benzoyl-β-phenylalanine (Va) (yield 90%; m.p. 83-85°), α-benzoyl-β-(p-methoxyphenyl)alanine (Vb) (yield quantitative; m.p. 55-56°, from aqueous methanol) and α-benzoyl-β-(3,4-methylenedioxyphenyl)alanine (Vc) (yield 93%; m.p. 101-103°).

SUMMARY

1. A general method was developed for the synthesis of β-aryl-α-benzamidoacrylhydroxamic acids involving the reaction of 2-phenyl-4-arylideneoxazolones with hydroxylamine acetate in methanol at pH 5-6.5 (yields 70-90%). It was shown that this method is also suitable for the synthesis of β-alkyl-α-benzamidoacrylhydroxamic acids.

2. The catalytic hydrogenation of β-aryl-α-benzamidoacrylhydroxamic acids gave α-benzoyl-β-arylalanylhydroxamic acids.

3. The structure of the obtained compounds was shown by their hydrolysis to α-benzoyl-β-arylalanines and their esters.

4. It was shown that the catalytic hydrogenation of α-benzamidocinnamic acids and their esters over palladium at room temperature and atmospheric pressure yields the corresponding α-benzoyl-β-arylalanines and their esters.

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DERIVATIVES OF BICYCLO[1,2,2]HEPTANE

V. 3-AMINOISOCAMPHANE AND RELATED COMPOUNDS

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A recent note [1] on the high physiological activity of 3-methylaminoisocamphane is of particular interest because among compounds of this type, substances with ganglion-blocking and hypotensive activity have not previously been known. In connection with prolonged researches in our laboratory [2,3] in search of physiologically active substances in the bicyclo[1,2,2]heptane series we also have developed a synthesis of 3-methylaminoisocamphane and for the purpose of obtaining new data on the variation of ganglionic blocking and hypotensive activity with structure in the bicyclo[1,2,2]heptane series, we have synthesized a number of other N-substituted 3-aminoisocamphanes. There is in the literature only a brief account of the synthesis of 3-methylaminoisocamphane by the action of hydrogen cyanide on camphane "under strongly acidic conditions at a temperature not above 5°" with subsequent reduction of the 3-formamidoisocamphane formed, by lithium aluminum hydride [4]. In this connection we made a detailed investigation of the behavior of camphane under the conditions of the Ritter reaction [5,6] at low temperatures, and it was found that camphane condenses with hydrogen cyanide in the presence of one mole of concentrated sulfuric acid at 0° in a medium of dibutyl ether, acetic acid or propionic acid, giving 3-formamidoisocamphane (I) in satisfactory yields, though it contains a considerable quantity (20%) of N-isoburnylformamide (II). Thus, in this case the reaction follows two directions:
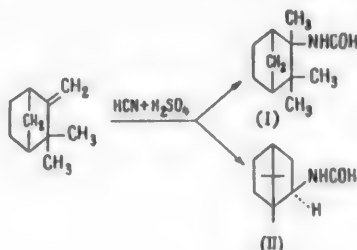
In order to minimize the formation of the isobornyl derivative it proved necessary to lower the temperature of the reaction mixture to -20 to -15° and allow a reaction time of 24 hours. Optimal reaction conditions were eventually found, that gave a yield of 3-formamidoisocamphane of more than 70%

R = H(I), CHCl₂, CCl₃
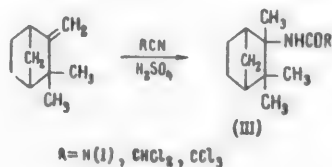
A disadvantage of the method is the necessity to use highly toxic hydrogen cyanide, which is particularly important where large-scale production is concerned. For this reason we examined other methods of synthesis of acyl derivatives of 3-aminoisocamphane, using the Ritter reaction. It is known that the reaction of camphene with aceto- and benzonitriles or with hydrogen cyanide under the Ritter reaction conditions at temperatures above 40° is accompanied by a Wagner rearrangement and leads to the corresponding N-acyl derivatives of iso-bornylamine [5,6]. The Wagner rearrangement takes place when the reaction between camphene and aceto- or benzonitrile is carried out at low temperatures (down to −50°) as we showed by special experiments. The condensation of camphene with benzyl thiocyanate under the Ritter reaction conditions at 0° also takes place with the Wagner rearrangement and leads to the corresponding N-isobornylcarbamate (II) [7]. According to the literature it is only with hydrogen cyanide at low temperatures that the normal condensation product (I) can be obtained. Thus, substitution of hydrogen cyanide by the above-mentioned nitriles brings about a marked change in the results of the reaction. The direction that the reaction follows is consequently strongly dependent on the nature of the cyanide taking part, and evidently the Wagner rearrangement does not take place when the nitrile group of the cyanide is highly active. It is well known that the nitrile groups in compounds containing strongly electronegative substituents in the α-position are of high activity. It would therefore be expected that by using dichloro- or trichloroacetonitrile in the Ritter reaction with camphene the same reaction product would be obtained as with hydrogen cyanide.

This idea was fully confirmed experimentally. On condensing camphene with dichloro- and trichloroaceto-nitrile in the presence of concentrated sulfuric acid at temperatures below 0°, 3-dichloroacetamidoisocamphane (III, R = CHCl$_2$) and 3-trichloroacetamidoisocamphane (III, R = CCl$_3$) were obtained in high yields. The acyl amino derivatives (III) (R= CHCl$_2$ or CCl$_3$) obtained on reduction with zinc in acetic acid or alcohol solution gave 3-acetamidoisocamphane (III, R = CH$_3$) which on hydrolysis by sodium hydroxide solution in a mixture of alcohol and ethylene glycol gave 3-aminoisocamphane.

(IV)
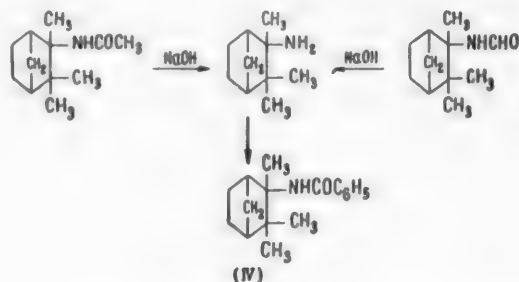
The benzoyl derivative of the latter (IV), prepared by the Schotten-Baumann method was completely identical with a sample of 3-benzamidoisocamphane prepared by benzoylation of the substance formed by the hydrolysis of the formyl derivative (I). This proves that the reaction between camphene and dichloro- or trichloro-acetonitrile does in fact give the 3-aminoisocamphane derivative, and the Ritter reaction in this case proceeds without a Wagner rearrangement. This fact is of interest in connection with the problem of the mechanism of the Ritter reaction, however, in view of the absence of any quantitative kinetic data it is not possible to express any conclusive opinons on this.

The 3-aminoisocamphane derivatives (I, III and IV) described above, form the starting materials for the synthesis of secondary amines of this series. On reducing them with lithium aluminum hydride, the corresponding 3-methyl- (V), 3-ethyl- (VI) and 3-benzylaminoisocamphane (VII) were obtained in high yields

R = H (V) , CH$_3$ (VI) , C$_6$H$_5$ (VII) .
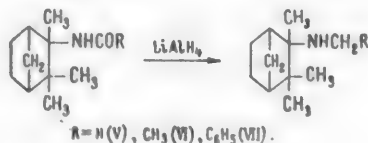
Relationship between structure and ganglionic blocking activity in the isocamphane amino- derivative series[*]

[*] The preparations were administered to cats intravenously without narcosis.

[**] A toxic phenomenon was observed — in- terruption of breathing.
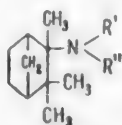
No.	R'	R''	Period of ac- tivity of 10 mg/kg doses (in hours)
1	H	H	18
2	H	CH_3	34
3	H	C_2H_5	18[***]
4	H	$CH_2C_6H_5$	0
5	CH_3	C_2H_5	9

It is interesting to note that when only a 50% excess of lithium aluminum hydride was used for the reduction of 3-benzamidoisocamphane (IV) the main reaction product proved to be 3-benzylideneaminoisocamphane, the hydro- lysis of which gave benzaldehyde and 3-aminoisocamphane. The desired reduction product (VII) could be obtained in satisfactory yield only when a 7-10-fold excess of lithium aluminum hydride was used.

The amines (V-VII), synthesized in this way, to - gether with 3-aminoisocamphane itself, in the form of their hydrochlorides, were subjected to pharmacological evaluation in order to follow the effect of the radical on the nitrogen atom on physiological activity. In order to examine the question of the effect of further substitu- tion in the amino group, 3-methylethylaminoisocamphane was prepared by methylation of 3-ethylaminoisocamphane.

The results of the evaluation, carried out in the Laboratory of Special Pharmacology of the Institute of Pharmacology and Chemotherapy of the Academy of Medical Sciences USSR, [*] are shown in the table. All the preparations lowered the blood pressure in conformity with the periods of ganglionic blocking activity.

Examination of the table shows that 3-aminoiso- camphane (No. 1) possesses a strong ganglionic blocking activity, considerably greater than the previously known gangliolytics — pentamine [bis(bromoethylate) of sym- N, N, N-pentamethyldiethylenetriamine] and hexone (hexamethylene bis-triethylammonium iodide). This ac- tivity is almost doubled on passing to 3-methylaminoisocamphane (No. 2). Further enlargement of radical R" leads, in the case of 3-ethylaminoisocamphane, to a decrease in activity and at the same time, marked toxicity of the preparation arises. In the case of 3-benzyl-aminoisocamphane (No. 4), the ganglionic blocking activity disappears. The change from secondary amines (Nos. 2 and 3) to tertiary (No. 5) is accompanied by considerable loss of ac- tivity (2-6 times).

EXPERIMENTAL

3-Formamidoisocamphane (I). 200 g of camphene was dissolved at -10-$0°$ in 80 ml of propionic acid and 20.0 g of potassium cyanide was added to the resulting solution at the same temperature over a period of 0.5 hour, with vigorous stirring. The mixture was then cooled to $-20°$ and 25 ml of 98% sulfuric acid was added dropwise with vigorous stirring over a period of 2 hours, keeping the temperature below $-15°$. The reaction was kept at this temperature for 24 hours after which it was poured on to 500 g of finely ground ice, the aqueous layer was separated from the oily material floating on the surface by means of a siphon, 300 ml of water was added and the aqueous solution was neutralized with sodium bicarbonate. After 1-2 hours the product (I) (26.0 g) that crystallized out was filtered off, washed on the filter with water and dried in a vacuum desiccator over phosphorus pentoxide (m.p. 128-135°). After recrystallizing from petroleum ether (b.p. 70-100°) 18.5 g (76%) of a colorless, crystalline material, m.p. 157-160°[**] was obtained; after three recrystallizations, m.p. 173-176°. According to the literature: m.p. 173-176° [4].

3-Dichloroacetamidoisocamphane (III, R= $CHCl_2$). 20 ml of 98% sulfuric acid was added with stirring, at a temperature not above $-15°$, over a period of 1-1.5 hours to a solution of 44.3 g of camphene and 43.0 g of

[*] The authors take this opportunity of expressing their deep gratitude to Yu. V. Uranov for placing the experi- mental results at their disposal.

[**] The 3-formamidoisocamphane of m.p, 157-160 was fairly pure because on reduction it gave 3-methylamino- isocamphane in high yield, identical with that described.

dichloroacetonitrile in 20 ml of propionic acid. The reaction mixture was kept for 2 days at-20 to −15°,after which it was poured on to 300 ml of ice water, the aqueous solution neutralized with sodium carbonate, the crystalline precipitate filtered off and dried in a vacuum desiccator over phosphorus pentoxide. After recrystallizing from 150 ml of petroleum ether (b.p. 70-100°),50.2 g of material of m.p. 106-108° was obtained; a further 10 g of the material was isolated from the mother liquor by evaporation of part of the solvent and recrystallization. Total yield 60.2 g (69.7%).

Found %: C 54.66, 54.55; H 7.30, 7.29. $C_{12}H_{19}ONCl_2$. Calculated %: C 54.55; H 7.25.

Colorless crystals, readily soluble in ether, alcohol and benzene, difficultly soluble in petroleum ether.

3-Trichloroacetamidoisocamphane (III, R = CCl₃). This was prepared in a similar way, as described in the previous experiment, from 122 g of camphene, 136 g of trichloroacetonitrile and 50 ml of 98% sulfuric acid in 100 ml of glacial acetic acid. The reaction product was distilled, the fraction boiling at 165-170° (1.5-2 mm) being collected. Yield 160 g. The product was reduced to 3-acetamidoisocamphane (III, R = CH₃) without further purification.

3-Acetamidoisocamphane (III, R = CH₃). A. 200 g of zinc dust was added in small portions, with stirring, to a solution of 160 g of 3-trichloroacetamidoisocamphane in 600 ml of glacial acetic acid, care being taken not to allow the temperature of the reaction mixture to rise above 80°. At the end of the exothermic period,the mixture was heated, with stirring, on a boiling water bath for 1 hour, the precipitate was then filtered off, the filtrate diluted with 1 500 ml of water, the aqueous layer separated from the supernatant oily material by means of a siphon, diluted with a further 1 000 ml of water and the aqueous solution neutralized with sodium carbonate. The 3-acetamidoisocamphane, that crystallized out after some time, was filtered off, washed on the filter with water, dried in a vacuum desiccator over phosphorus pentoxide and recrystallized from petroleum ether (b.p. 70-100°). Yield 68.0 g; m.p. 131-132°. Mixed melting point with N-isobornylacetamide (m.p. 140-141°) − 102-104°.

B. 20.0 g of zinc dust was added to a solution of 6.0 g of 3-dichloroacetamidoisocamphane in 50 ml of glacial acetic acid and the mixture was heated at 80-90° for 6 hours. 3-Acetamidoisocamphane was isolated and purified as described above. Yield 3.2 g (72%); m.p. 131-132°.

Found % C 73.70 , 73.81; H 11.05, 11.04. $C_{12}H_{21}ON$. Calculated %: C 73.79; H 10.84.

Colorless crystals, readily soluble in ether, alcohol and benzene, soluble with difficulty in petroleum ether.

3-Aminoisocamphane. 10 g of 3-acetamidoisocamphane was added to a solution of 20 g of sodium hydroxide in a mixture of 100 ml of ethylene glycol and 15 ml of ethanol and the solution obtained was refluxed for 50 hours. The reaction mixture was then steam distilled, the distillate extracted with ether, the ethereal extract dried over sodium hydroxide, evaporated to 50 ml and saturated with dry hydrogen chloride; 3-aminoisocamphane hydrochloride separated and was filtered off, washed on the filter with absolute ether and dried in a vacuum desiccator over solid alkali. Yield 5.1 g (52.5%); decomposition temperature ∼ 320° (rapid heating).

Found %: Cl 18.66, 18.83. $C_{10}H_{20}NCl$. Calculated %: Cl 18.69.

The mother-liquor from the 3-aminoisocamphane hydrochloride was washed with bicarbonate solution, dried over calcium chloride and the solvent was distilled off. The residue yielded 4.0 g (40%) of the initial 3-acetamidoisocamphane; m.p. 130-131°.

3-Benzamidoisocamphane. A. 5.1 g of 3-aminoisocamphane hydrochloride was dissolved in 20 ml of water, 10% aqueous alkali was added and the amine that separated was benzoylated by the addition of benzoyl chloride. The 3-benzamidoisocamphane that separated was filtered off, washed on the filter with 10% alkali and water, and recrystallized from 60% ethanol. Yield 6.5 g (98%); m.p. 122-123°.

B. 1.0 g of 3-formamidoisocamphane of m.p.157-160° was hydrolyzed by refluxing for 50 hours with 3 g of sodium hydroxide in 20 ml of ethylene glycol and 5 ml of ethanol. The solution was then diluted with 100 ml of water and the 3-aminoisocamphane and 3-formamidoisocamphane were extracted with ether, the ethereal extract was washed with 30 ml of 5% hydrochloric acid, the aqueous portion made alkaline and the amine that separated was benzoylated by the Schotten-Baumann method. Yield of 3-benzamidoisocamphane, 0.74 g (46.4%); m.p. 122-123° (from aqueous alcohol). A mixture of the products from methods A and B gave no melting point depression. According to the literature m.p. 125° [8].

Found %: C 79.06, 79.08; H 9.22,9.16. $C_{17}H_{25}ON$. Calculated %: C 79.33; H 9.14.

3-Methylaminoisocamphane (V). 11.7 g of 3-formamidoisocamphane, of m.p. 157-160°, was added to a solution of lithium aluminum hydride prepared from 32 g of lithium hydride and 27.0 g of aluminum bromide in 100 ml of absolute ether and the mixture was refluxed gently with stirring for 5-6 hours. The reaction mixture was then cooled in ice-water and 200 ml of 40% aqueous sodium hydroxide was added. The ethereal layer was separated, the aqueous layer extracted 3-5 times with ether, and the extracts, combined with the main portion, were dried over solid alkali. After removal of the solvent the residue was distilled, the fraction boiling at 95-96° (10 mm) being collected. Yield 9.8 g (92%).

n_D^{20} 1.4875. From [4]: b.p. 72° (4 mm), n_D^{20} 1.4881.

The hydrochloride was prepared in ether, the yield was quantitative.

B.p. 243-245° (decomp.).From [4]: b.p. 243-246° (decomp.).

Found %: Cl 17.35, 17.32. $C_{11}H_{22}NCl$. Calculated %: Cl 17.49.

3-Ethylaminoisocamphane (VI). This was prepared similarly by the reduction of 9.5 g of 3-acetamido-isocamphane for 6 hours with lithium aluminum hydride (from 3.2 g of lithium hydride and 27.0 g of aluminum bromide in 140 ml of absolute ether). The dried ethereal extracts were evaporated to 40-50 ml and saturated with dry hydrogen chloride. The 3-ethylaminoisocamphane hydrochloride that precipitated was filtered off, washed with absolute ether and recrystallized from absolute alcohol. Yield, 9.0 g (85.4%); m.p. 254-255°.

Found %: Cl 16.45; 16.43. $C_{12}H_{24}NCl$. Calculated %: Cl 16.28.

Colorless plates, soluble with difficulty in cold water and in alcohol; insoluble in ether.

3-Benzylaminoisocamphane (VII). This compound was synthesized and isolated in the form of the hydrochloride in a similar manner to that described above. 4.0 g of 3-benzamidoisocamphane was reduced with lithium aluminum hydride (1.0 g of lithium hydride and 8.0 g of aluminum bromide in 50 ml of absolute alcohol by means of ether, 3.1 g (74%) of 3-benzylaminoisocamphane of m.p. 198-198.5° was obtained.

Found %: Cl 12.55, 12.48. $C_{17}H_{26}NCl$. Calculated %: Cl 12.67.

Colorless crystals, moderately soluble in water, readily soluble in alcohol and of poor solubility in ether.

3-Methylethylaminoisocamphane. 40 ml of 10% sodium hydroxide solution was added to a suspension of 5.0 g of 3-ethylaminoisocamphane hydrochloride in 50 ml of ether and the mixture was shaken until the solid hydrochloride had completely disappeared. The ethereal solution of 3-ethylaminoisocamphane obtained was dried over alkali, filtered and the solvent removed. The base obtained was mixed with 10 ml of methyl iodide, after 24 hours the mixture was diluted with 30 ml of absolute ether and the precipitate formed was filtered off (5.2 g), this was dissolved in water, 40% alkali solution was added to give a distinct alkaline reaction and the base that separated was treated with 15 ml of acetyl chloride to remove unreacted secondary amine. The acetyl derivative formed and the tertiary amine were then extracted with ether, the ethereal extracts dried over solid alkali, filtered and evaporated to 20 ml. Saturation of the ethereal solution obtained, with dry hydrogen chloride, yielded 2.0 g of 3-methylethylaminoisocamphane of m.p. 238-240°. After recrystallization from absolute alcohol, m.p. 245-247°.

Found %: Cl 15.57. $C_{13}H_{26}NCl$. Calculated %: Cl 15.30.

Colorless leaves, readily soluble in water and aqueous alcohol, moderately soluble in absolute alcohol, and insoluble in ether.

SUMMARY

1. The synthesis of some derivatives of 3-aminoisocamphane has been achieved and the question of the relationship between physiological activity and structure in this series of compounds is discussed.

2. It is shown that trichloro- and dichloroacetonitrile react with camphene under the conditions of the Ritter reaction, at low temperatures, without a Wagner rearrangement taking place.

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THE ACTION OF MERCURY SALTS ON 2-METHYL-4-PHENYLBUTYNE-3-DIOL-1,2

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The reactions with mercuric chloride and with sulfuric acid of α-glycols of the acetylenic series, containing a primary and tertiary hydroxyl group, have been studied previously for the case of 2,4-diphenylbutyne-3-diol-1,4 (unsym-phenyl-phenylacetylenylethylene glycol) [1]. From this glycol, 2,4-diphenylfuran was obtained by the action of mercuric chloride in alcoholic solution, whereas sulfuric acid in alcoholic solution converted this glycol to its half ether — 2,4-diphenyl-2-ethoxybutyne-3-ol-1 and partly to 2,4-diphenylfuran.

By the action of a mercury salt on an acetylenic glycol with a secondary and a tertiary hydroxyl group — 2-methyl-1,4-diphenylbutyne-3-diol-1,2 — one of us in collaboration with É. D. Venus-Danilova [2] isolated an intermediate product from the reaction between the glycol and mercuric chloride — 3-methyl-2,5-diphenyl-4-chloromercurifuran, which subsequently became converted to 3-methyl-2,5-diphenylfuran.

In the case of other secondary-tertiary acetylenic α-glycols —3-methyl-5-phenylpentyne-4-diol-2,3 and 1,2,4-triphenylbutyne-3-diol-1,2 — no intermediate products were isolated from the reaction with mercuric chloride, but only the end products of the reaction were examined — 2,3-dimethyl-5-phenylfuran and 2,3,5-triphenylfuran [3,4].

For the purpose of examining the possibility of forming similar, intermediate, β-mercurated furan derivatives from the reaction between mercuric chloride and primary-tertiary, acetylenic α-glycols also, we have investigated the reaction between uns-methylphenylacetylenylethylene glycol (2-methyl-4-phenylbutyne-3-diol-1,2) (I) and mercuric chloride. The glycol (I) was prepared by the Zh. I. Iotsich reaction from acetol and phenylacetylenyl magnesium bromide.

A preliminary experiment on the action of mercuric chloride on the acetylenic glycol (I) (in equimolar ratio) under the conditions used previously [2] showed that the crystalline precipitate that appeared initially disappeared rapidly on warming and the final product consisted of 4-methyl-2-phenylfuran (III) contaminated with the organomercury compound.

The comparatively low yield of 4-methyl-2-phenylfuran (46.8%) can be explained,presumably, by partial mercuration of the 4-methyl-phenylfuran formed, which contains no substituent in the α-position. The substituted furans prepared previously [2-4] contained radicals in the α-position.

It is known from the literature [5] that mercury adds on to the β-position in furan with considerably more difficulty than to the α-position. The preparation by L. A. Pavlova [1] of 2,4-diphenylfuran in higher yield by the action of mercuric chloride on 2,4-diphenylbutyne-3-diol-1,2 is evidently explained by the lower reactivity of 2,4-diphenylfuran in comparison with 4-methyl-2-phenylfuran.

In order to avoid the side reaction of mercuration of 4-methyl-2-phenylfuran, hydrochloric acid was added in an experiment on the reaction of the acetylenic glycol (I) with mercuric chloride, in this case 4-methyl-2-phenylfuran was obtained in the pure state and in higher yield (65%). However, it was not possible to increase the yield further because of the sensitivity of this furan (III) to strong acid. Although addition of hydrochloric acid eliminates mercuration of furan (III) to the α-chloromercurifuran (IV) it also promotes partial resinification of the furan (III).

The crystalline material that separates immediately when equimolar, alcoholic solutions of 2-methyl-4-phenylbutyne-3-diol-1,2 and of mercuric chloride are mixed at room temperature without addition of hydrochloric acid, contains chlorine and mercury but no hydroxyl group is detected. On heating in the presence of hydrochloric acid it forms 4-methyl-2-phenylfuran (III),which has been described in the literature [6]. From analysis and from this conversion to 4-methyl-2-phenylfuran it can be stated that the first product from the reaction between 2-methyl-4-phenylbutyne-3-diol-1,2 (I) and mercuric chloride is the β-mercurated furan — 4-methyl-2-phenyl-3-chloromercurifuran (II). This compound is isomeric with the α-mercurated 4-methyl-2-phenyl-5-chloromercurifuran (IV) [6] prepared by us by the action of mercuric chloride on 4-methyl-2-phenylfuran in the presence of sodium acetate.
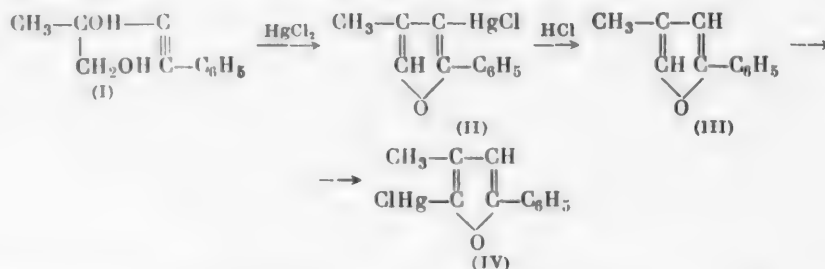
β-Mercurated furans which do not contain a substitutent at one of the α-positions are comparatively rare compounds because direct mercuration of furans leads to the formation of α-chloromercurifurans. Previously there was only one method for the preparation of β-chloromercurifurans, through the mercury salt of the corresponding carboxylic acid (of the pyromucic acid type) [7]. This reaction of primary-tertiary and secondary-tertiary acetylenic α-glycols is a new, convenient method for the preparation of the corresponding β-chloromercurifurans and furthermore it confirms the general scheme of reaction between acetylenic α-glycols and mercury salts put forward by E. D. Venus-Danilova and one of us [2].

In addition to mercuric chloride the action of mercuric sulfate and of sulfuric acid on alcoholic solutions of the glycol (I) was also studied. In the first case a small quantity of sulfuric acid was added to suppress the mercuration reaction; formation of the intermediate product was not observed and only 4-methyl-2-phenylfuran was isolated. In the second case, in contrast to the transformation of phenyl-phenylacetylenylethylene glycol [1], our glycol (I) remained unchanged.

EXPERIMENTAL

Preparation of 2-Methyl-4-Phenylbutyne-3-Diol-1,2 (Uns-Methylphenylacetylenyl-ethylene Glycol) (I).

37 g of freshly distilled acetol [8] was added with stirring and water cooling to an ethereal solution of phenylacetylenylmagnesium bromide prepared in the usual way (from 30 g of magnesium, 140 g of ethyl bromide and 125 g of phenylacetylene). On the following day the product was decomposed with dilute hydrochloric acid and the ethereal extract was washed with sodium carbonate solution and water. The glycol separated partially on washing the ethereal layer and for this reason it was found best to wash with warm water. After drying and cooling, the bulk of the glycol separated from the ether (38 g) and after removal of the ether a further 18 g of somewhat impure product was obtained. Recrystallization from ether yielded 52 g (59%) of the glycol, of m.p. 110-111°. This compound reacted vigorously with methylmagnesium iodide and decolorized potassium permanganate solution and a solution of bromine in chloroform, rather slowly. On heating with potassium carbonate [9] to 270°, phenylacetylene was liberated and was detected by its reaction with silver oxide in ammonia solution.

Found %: C 75.22, 75.23; H 6.87, 7.09; OH 19.60, M 183 (from Rast) $C_{11}H_{12}O_2$. Calculated %: C 75.00; H 6.81; OH 19.32. M 176.

Action of Mercuric Chloride on Uns-Methylphenylacetylenylethylene Glycol *

Experiment 1. On mixing an alcoholic solution of 5 g of the glycol with 7.7 g of mercuric acetate in 50 ml of 96% ethyl alcohol, a white, silky precipitate began to separate immediately and the whole mass rapidly thickened. On refluxing on the water bath, the precipitate dissolved and after refluxing for 2 hours the solution was poured into water, the product extracted with benzene and dried over sodium sulfate. The product was distilled in vacuo after removal of the benzene. 2.1 g of product of b.p. 120-122° (14 mm), which crystallized rapidly, was obtained. A considerable quantity of resin was left in the distillation flask, and mercury and mercuric chloride separated out towards the end of the distillation. After recrystallization from methyl alcohol the product, which had an odor reminiscent of that of diphenylmethane, melted at 42-43°. The product did not contain chlorine, mercury or hydroxyl groups and did not react with 2,4-dinitrophenylhydrazone.

Found %: C 88.18, 88.26; H 6.52, 6.48. M 160.8. $C_{11}H_{10}O$. Calculated %: C 88.51; H 6.37. M 158.

Judging by its properties and the analytical data, this material is 4-methyl-2-phenylfuran (III), which is described in the literature [6]. Yield 46.8%.

Mercuration of the 4-methyl-2-phenylfuran was carried out in order to confirm its structure and to elucidate the nature of the substance that crystallizes out in the early stages of the reaction, contains mercury, and is present as an impurity in the main product. Sodium acetate dissolved in 10 ml of methyl alcohol was added to a solution of 1 g of 4-methyl-2-phenylfuran and 1.5 g of mercuric chloride in 15 ml of ethyl alcohol. A crystalline precipitate soon began to separate and increased in quantity over a period of 24 hours. After recrystallization of the precipitate from methyl alcohol, colorless, needle-shaped crystals of m.p. 170-171° were obtained. A melting point of 171° is quoted in the literature [6] for 4-methyl-2-phenyl-5-chloromercurifuran but no analysis or evidence of structure was quoted for this substituted α-chloromercurifuran.

Found %: Hg 51.10, 51.24; Cl 8.82, 9.08. M 395 (From Rast) $C_{11}H_9OClHg$. Calculated %: Hg 51.01; Cl 9.02. M 393.

In view of the presence of a reactive α-position in 4-methyl-2-phenylfuran, the material of m.p. 170-171° must be considered to be the α-isomer, 4-methyl-2-phenyl-5-chloromercurifuran (IV).

When 4-methyl-2-phenylfuran (1 g) was allowed to stand for 1 month with maleic anhydride (1.5g) in 20 ml ether another condensation product was obtained in the form of colorless crystals, decomposing at 166-169°.

Found %: C 70.30; H 4.77. $C_{15}H_{12}O_4$. Calculated %: C 70.31; H 4.69.

Thus the end product of the reaction between mercuric chloride and the actylenic glycol (I) is 4-methyl-2-phenylfuran.

Experiment 2. The preceding experiment was repeated starting from 1 g of the acetylenic glycol (I) and 1.35 g of mercuric chloride. The benzene extract was divided into two portions. In the first portion 0.04 g of mercury was found, indicating the presence of 15% of the α-mercurated furan (IV). On evaporating the bulk of the benzene from the second portion, a small quantity of crystalline material of m.p. 170° (from methyl alcohol) separated, this gave no melting point depression with 4-methyl-2-phenyl-5-chloromercurifuran (IV) prepared by the action of mercuric chloride on 4-methyl-2-phenylfuran (III) in the presence of sodium acetate (Experiment 1).

Hence, the main product from the reaction of the acetylenic glycol (I) with mercuric chloride is 4-methyl 2-phenylfuran (III) contaminated with its mercurated product — the α-chloromercurifuran (IV).

Experiment 3. Experiment 2 was repeated, but with the addition of 1 ml of concentrated hydrochloric acid in 10 ml of ethyl alcohol to the reaction mixture. Only a trace of mercury (0.0025 g) was found in the benzene extract. This indicates that hydrochloric acid retards the mercuration of 4-methyl-2-phenylfuran because the quantity of the α-chloromercurifuran impurity is reduced from 15 to 0.5 %.

Experiment 4. Experiment 1 was repeated but with the addition of 5 ml of concentrated hydrochloric acid; in these circumstances the characteristic odor of 4-methyl-2-phenylfuran arose immediately. 2.9 g (64.6%) of 4-methyl-2-phenylfuran of b.p. 119-121° (13 mm), m.p. 43-44°, was isolated.

Hence, hydrochloric acid accelerates the decomposition of 4-methyl-2-phenyl-3-chloromercurifuran (II)

*All experiments were carried out in a flask with a reflux condenser, with stirring.

(the initial product from the reaction of the glycol with mercuric chloride) and increases the yield of 4-methyl-2-phenylfuran, retarding its mercuration to the α-chloromercurifuran (IV).

Experiment 5. From 5 g of the glycol, 1.9 g of mercuric chloride (1:0.25 moles), 50 ml of alcohol and 5 ml of concentrated hydrochloric acid, 2.85 g (63.6%) of 4-methyl-2-phenylfuran were obtained under the conditions of Experiment 4.

Thus, a reduction in the quantity of mercuric chloride does not affect the yield of 4-methyl-2-phenylfuran.

Experiment 6 was carried out with the object of isolating the primary product formed in the reaction between the glycol and mercuric chloride. By mixing solutions of 5 g of the glycol and 7.7 g of mercuric chloride in a total volume of 50 ml of ethyl alcohol and allowing the mixture to stand for 3 hours at room temperature a light, lustrous, crystalline precipitate was obtained, which was washed on the filter with a small quantity of alcohol. 6.2 g of a colorless substance was isolated in the form of thin, long needles, dissolving readily in acetone and with difficulty in cold benzene and alcohol. After recrystallization the material did not melt up to 200°, above this temperature it gradually darkened and charred, it contained chlorine and mercury and did not contain hydroxyl groups. On refluxing with alcohol for 1 hour (2 g of product + 20 ml of alcohol) it remained unchanged and crystallized out on cooling. On adding hydrochloric acid (1 ml) to a suspension of the material in alcohol, the odor of 4-methyl-2-phenylfuran arose immediately. After heating and adding sodium acetate (3 g in 10 ml of water) to the solution a crystalline material of m.p. 170-171° (from alcohol) was isolated, giving no melting-point depression with the product obtained by the action of mercuric chloride on 4-methyl-2-phenylfuran.

Found %: Hg 51.20, 50.96; Cl 9.14, 9.00 M 381 (from Rast) $C_{11}H_9ClHg$.   Calculated %: Hg 51.01; Cl 9.02. M 393.

Judging from its properties and from the analytical data, the product is the β-chloromercurifuran, not described in the literature — 4-methyl-2-phenyl-3-chloromercurifuran (II) — isomeric with 4-methyl-2-phenyl-5-chloromercurifuran prepared by direct mercuration of 4-methyl-2-phenylfuran. Yield, quantitative.

Action of Mercuric Sulfate on Uns-Methylphenylacetylenylethylene Glycol

Two experiments were carried out starting from 5 g of the glycol and 2.1 g of mercuric sulfate (1:0.25 moles) and from 5 g of the glycol and 4.2 g of mercuric sulfate (1:0.5 moles). The quantity of alcohol in both experiments was 50 ml. In order to eliminate mercuration of the furan (III), 1 ml of sulfuric acid was added. The bulk of the mercuric sulfate did not dissolve. After refluxing for 2 hours the precipitate was filtered off and washed with benzene. The alcoholic solution was diluted with water and extracted wtih benzene and after evaporation of the solvent and distillation of the residue in vacuo, 2.5 g (55.7%) of 4-methyl-2-phenylfuran of m.p. 43-44° was obtained in both cases.

Hence, in this case again a substituted furan is obtained from the glycol and the quantity of mercuric sulfate taken does not affect the yield of product.

SUMMARY

1. A primary-tertiary acetylenic α-glycol — uns-methylphenylacetylenylethylene glycol (2-methyl-4-phenylbutyne-3-diol-1,2), that has not previously been described in the literature, has been synthesized and its reaction with mercuric chloride and sulfate has been studied.

2. It was found that in the reaction with mercuric chloride this glycol forms as an intermediate product a β-mercurated furan — 4-methyl-2-phenyl-3-chloromercurifuran, isomeric with the α-mercurated furan, 4-methyl-2-phenyl-5-chloromercurifuran.

3. A new, convenient method has been found for the preparation of β-mercurated furans, not substituted in the α-position, which cannot be prepared by direct mercuration of furans and which consequently are not readily available compounds.

4. The scheme previously suggested for the reaction between secondary-tertiary acetylenic α-glycols and mercuric salts has been confirmed.

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RESEARCHES IN THE QUINONE FIELD XXIV. THE ISOMERIZATION OF ADDUCTS OF p-QUINONES WITH DIENIC HYDROCARBONS

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The isomerization of adducts of p-quinones with dienic hydrocarbons is a valuable method for the synthesis of substituted hydroquinones.
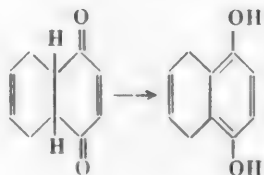
According to our findings, the method described in the literature [1,2] of isomerizing the adducts with hydrobromic acid is not suitable for the isomerization of large amounts of these compounds (greater than 5-10 g). It is stated in patents [3, 4] that isomerization of the adduct of toluquinone and butadiene is carried out with hydrochloric acid in aqueous-alcoholic solution or with 3% sodium hydroxide in the absence of air. G. I. Ostrozhenskaya [5] isomerized this adduct by boiling with water after first washing out traces of acetic acid that had been used as solvent in the condensation of the toluquinone with butadiene.

(I) $R_1, R_2, R_3, R_4 = H$
(II) $R_1, R_2, R_4 = H$; $R_3 = CH_3$
(III) $R_1 = CH_3$; $R_2, R_3, R_4 = H$
(IV) $R_1, R_2 = H$; $R_3, R_4 = CH_3$
(V) $R_1 = Cl$; $R_2, R_3, R_4 = H$
(VI) $R_1, R_2 = Cl$; $R_3, R_4 = H$
(VII) $R_1, R_2 = Cl$; $R_3 = H$; $R_4 = CH_3$

(VIII) $R_1, R_2 = H$; $R_3, R_4 = CH_3$
(IX) $R_1, R_3, R_4 = CH_3$; $R_2 = H$
(X) $R_1 = H$; $R_2, R_3, R_4 = CH_3$

(XI)

In this work we set out to isomerize the adducts by refluxing them in acetic acid. This method, which we had already used to prepare 2-methyl-5,8-dihydro-5,8-endoethylenenaphthohydroquinone and 1,4-dihydro-1,4-endoethyleneanthrahydroquinone [6], enables the condensation of quinones with dienic hydrocarbons, and isomerization of the adducts formed to substituted hydroquinones, to be carried out without isolation of the adducts.

The following compounds were prepared in the course of this work: 5,8-dihydronaphthohydroquinone (I), 6-methyl-5,8-dihydronaphthohydroquinone (II), 2-methyl-5,8-dihydronaphthoquinone (III), 6,7-dimethyl-5,8-dihydronaphthoquinone (IV), 2-chloro-5,8-dihydronaphthoquinone (V), 2,3-dichloro-6-methyl-5,8-dihydronaphthoquinone (VI), 2,3-dichloro-6-methyl-5,8-dihydronaphthoquinone (VII), 2,3-dimethyl-1,4,-4-dihydroanthrahydroquinone (VIII), 2,3,5-trimethyl-1,4-dihydroanthrahydroquinone (IX), 2,3,6-trimethyl-1,4-dihydroanthrahydroquinone (X) and 6-methyl-1,4-dihydro-1,4-endoethyleneanthrahydroquinone (XI).
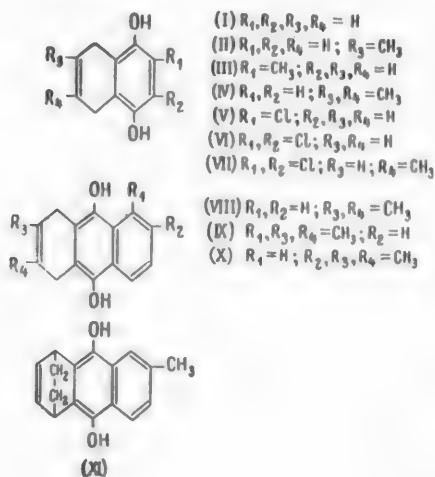
TABLE 1

Preparative Conditions and Properties of the Hydroquinones

Experiment No	Starting materials	Starting materials wt. (in g)	Quantity of acetic acid (in ml)	Reflux time	Hydroquinone obtained	Yield (in g)	Melting point		Found		Calculated %	
							Found	Quoted in literature	C	H	C	H
1	p-Benzoquinone / Butadiene	108 / 108	500	2 hours	5,8-Dihydronaphthohydroquinone (I)	145	210—211°	212° [7]	—	—	—	—
2	p-Benzoquinone / Isoprene	10.8 / 10.8	50	1.5 hours	6-Methyl-5,8-dihydronaphthohydroquinone (II)	14.6	164—166	—	74.99, 75.11	7.05, 7.08	74.97	6.86
3	Toluquinone / Butadiene	12.2 / 10.8	50	1.5 hours	2-Methyl-5,8-dihydronaphthohydroquinone (III)	16.5	167—168	168 [5]	—	—	—	—
4	Adduct of p-benzoquinone and 2,3-dimethyl-butadiene*	15	50	20 min	6,7-Dimethyl-5,8-dihydronaphthohydroquinone (IV)	12.8	207—208	—	75.32, 75.45	7.77, 7.49	75.76	7.42
5	Chloro-p-benzoquinone / Butadiene	2.5 / 1.9	20	2 hours	2-Chloro-5,8-dihydronaphthohydroquinone (V)	2.15	141	141 [8]	—	—	—	—
6	2,3-Dichloroquinone / Butadiene	2.5 / 1.5	20	3 hours	2,3-Dichloro-5,8-dihydronaphthohydroquinone (VI)	3.5	163—164	—	52.32, 52.09	3.69, 3.69	51.96	3.43
7	2,3-Dichloroquinone / Isoprene	2.5 / 1.9	20	3 hours	2,3-Dichloro-6-methyl-5,8-dihydroanthrahydroquinone (VII)	2.5	144—145	—	54.22, 54.42	4.40, 4.47	54.34	4.11
8	Adduct of naphthoquinone and 2,3-dimethylbutadiene [9]	3	30	40 min	2,3-Dimethyl-1,4-dihydroanthrahydroquinone (VII)	2.5	198—199	—	79.67, 79.79	6.73, 6.68	79.97	6.71
9	Adduct of 5-methylnaphthoquinone and 2,3-dimethyl-butadiene [9]	7	70	40 min	2,3,5-Trimethyl-1,4-dihydroanthrahydroquinone (IX)	5	166—168	—	80.50, 80.21	6.97, 6.94	80.28	7.13
10	Adduct of 6-methyl-naphthoquinone and 2,3-dimethylbutadiene	3	30	40 min	2,3,6-Trimethyl-1,4-dihydroanthrahydroquinone (X)	2.4	225—226	—	80.35, 80.21	7.02, 7.09	80.28	7.13
11	Adduct of 6-methylnaphthoquinone and cyclohexadiene	5.5	5	2 hours	6-Methyl-1,4-dihydro-1,4-endoethyleneanthrahydroquinone (XI)	4.85	117—120	—	81.07, 80.96	6.12, 6.12	80.92	6.39

*The adduct of p-benzoquinone and 2,3-dimethylbutadiene was prepared by heating a mixture of 10.8 g of p-benzoquinone, 11.25 g of 2,3-di-methylbutadiene and 100 ml of water at 40° for 2.5 hours with good stirring.

TABLE 2

Adducts of 5- and 6-Methylnaphthoquinones with 2,3-Dimethylbutadiene and of 6-Methylnaphthoquinone with Cyclohexadiene-1,3

Starting materials	Wt. of starting material (in g)	Adduct obtained	Yield (g)	Melting point	Found (%)		Calculated (%)	
					C	H	C	H
5-Methylnaphthoquinone 2,3-Dimethylbutadiene	8 8	Adduct of 5-methylnaphthoquinone 2,3-dimethylbutadiene (XII)*	7	77—78°	80.15, 80.25	6.85, 6.86	80.28	7.13
6-Methylnaphthoquinone 2,3-Dimethylbutadiene	5 5	Adduct of 6-methylnaphthoquinone 2,3-dimethylbutadiene (XIII) *	5.6	119—120	80.22, 79.99	7.15, 7.04	80.28	7.13
6-Methylnaphthoquinone Cyclohexadiene-1,3	3.67 6.23	Adduct of 6-methylnaphthoquinone and cyclohexadiene-1,3 (XIV)**	5	80—82	81.25, 80.06	6.58, 6.57	80.92	6.39

*Adduct prepared by the method described for the preparation of the adduct of naphthoquinone and 2,3-dimethylbutadiene [9].

**Adduct prepared by the method described for the preparation of the adduct of naphthoquinone and cyclohexadiene [7].

The quantities of reagents and reaction times as well as the melting points, yields and analyses of the hydroquinones enumerated above are given in Table 1.

The adducts of 5-methylnaphthoquinone and 2,3-dimethylbutadiene (XII), of 6-methylnaphthoquinone and 2,3-dimethylbutadiene (XIII) and of 6-methylnaphthoquinone and cyclohexadiene (XIV) were prepared for the first time. The yields, melting points and analyses of these adducts are given in Table 2.

(XII) $R_1, R_3, R_4 = CH_3$; $R_2 = H$
(XIII) $R_1 = H$; $R_2, R_3, R_4 = CH_3$

(XIV)
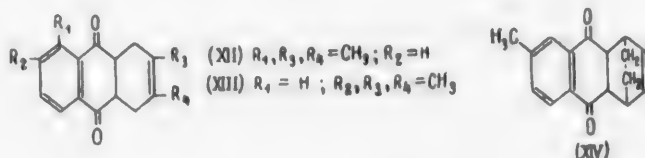
EXPERIMENTAL *

5,8-Dihydronaphthohydroquinone(I). 500 ml of acetic acid was saturated with 108 g of butadiene in a thick-walled glass flask, cooled in ice. 108 g of p-benzoquinone was added to the solution formed. The reaction vessel was sealed and allowd to stand for 42 hours at room temperature, after which the solution was heated in a flask under reflux for 2 hours at the boiling point of acetic acid. The crystalline 5,8-dihydronaphthohydroquinone (I) that separated on cooling was separated and dried.

Experiments 2,3,5,6 and 7 were carried out under the conditions described above.

2,3,5-Trimethyl-1,4-dihydroanthrahydroquinone (IX). For the isomerization of the adduct of 5-methylnaphthoquinone and 2,3-dimethylbutadiene-1,3 (XII) to the hydroquinone (IX), 7 g of the adduct (XII) was refluxed in 70 ml of acetic acid. The hydroquinone (IX) is a white crystalline material, rapidly darkening in the air. The yield and melting point are given in Table 1.

Experiments 4, 8, 10 and 11 were carried out similarly.

SUMMARY

A new preparative method for the isomerization of adducts of p-quinones and dienic hydrocarbons to substituted hydroquinones, has been developed.

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*Carried out with the assistance of V. K. Lomova.
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RESEARCHES IN THE QUINONE FIELD. XXV.

SYNTHESIS OF NAPHTHOQUINONES AND DIHYDROANTHRAQUINONES

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In one of our papers it was shown that the most convenient method for the preparation of 1,4-naphtho-quinone and 2-methyl-1,4-naphthoquinone is by synthesis from p-benzoquinone (toluquinone) and butadiene where the reaction is carried out without isolation of the adducts from which the hydroquinones are obtained by isomerization [1].

In this work 6-methylnaphthoquinone (I) and 5-methylnaphthoquinone (II) were prepared by the same method. 6,7-Dimethyl-1,4-naphthoquinone (III) was prepared in good yield by the oxidation of 6,7-dimethyl-5,8-dihydronaphthohydroquinone [2] with chromic acid. 2,3-Dichloronaphthoquinone (IV) was obtained from 2,3-dichloro-p-benzoquinone and butadiene.

(I) R_1, R_3, R_4, R_5 = H; R_2 = CH$_3$.
(II) R_1 = CH$_3$; R_2, R_3, R_4, R_5 = H.
(III) R_1, R_4, R_5 = H; R_2, R_3 = CH$_3$.
(IV) R_1, R_2, R_5 = H; R_4, R_3 = Cl.
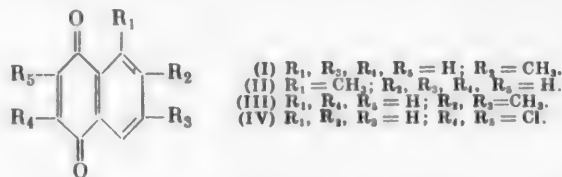
In addition, some of the hydroquinones characterized in the previous communication [2] were oxidized with potassium bromate in an acidic medium. 6-Methyl-1,4-dihydro-1,4-endoethyleneanthraquinone (V), 6,7-dimethyl-1,4-dihydro-1,4-endoethyleneanthraquinone (VI), 2,3-dimethyl-1,4-dihydroanthraquinone (VII), 2,3,5-trimethyl-1,4-dihydroanthraquinone (VIII) and 2,3,6-trimethyl-1,4-dihydroanthraquinone (IX) were obtained.

(V) R_1 = H ; R_2 = CH$_3$.
(VI) R_1 , R_2 = CH$_3$.

(VII) R_1, R_2 = CH$_3$; R_3, R_4 = H
(VIII) R_1, R_2, R_3 = CH$_3$; R_4 = H
(IX) R_1, R_2, R_4 = CH$_3$; R_3 = H
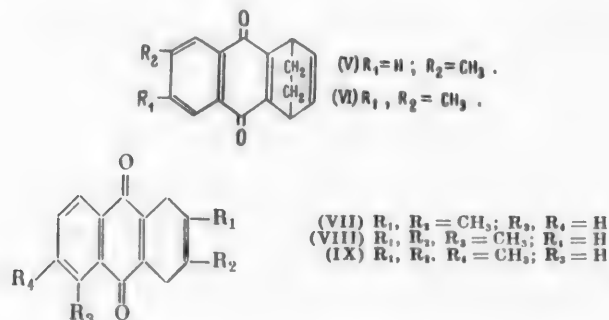
The experimental results on the preparation of the dihydroanthraquinones are given in the table.

Preparation of Quinones

Starting Material	Wt. of starting material (in g)	Oxidizing mixture				Quinone obtained	Yield (in g)	Melting point	Found %		Calculated (%)	
		Dioxan in ml	KBrO₃ (in g)	H₂SO₄ (in ml)	water (in ml)				C	H	C	H
6-Methyl-1,4-dihydro-1,4-endoethyleneanthra-hydroquinone	4.4	45	2.2	3.5	25	6-Methyl-1,4-dihydro-1,4-endoethyleneanthra-quinone (V)	3.3	137–138°	81.52, 81.82	5.38, 5.42	81.58	4.64
Adduct of 6,7-dimethyl-naphthoquinone and cyclo-hexadiene 1,3.	14.7	125	7.2	10	75	6,7-Dimethyl-1,4-dihydro-1,4-endoethyleneanthra-quinone (VI)	12	208–209	82.02, 82.08	6.36, 6.37	81.79	6.10
2,3-Dimethyl-1,4-di-hydroanthrahydroquinone	8	80	4	6.4	50	2,3-Dimethyl-1,4-dihydro-anthraquinone (VII)	6.7	202	81.27, 81.01	5.43, 5.64	80.64	5.92
2,3,5-Trimethyl-1,4-di-hydroanthrahydroquinone	5	50	2.5	4	30	2,3,5-Trimethyl-1,4-di-hydroanthraquinone (VIII)	3.2	173	81.31, 81.42	6.66, 6.75	80.92	6.39
2,3,6-Trimethyl-1,4-di-hydroanthrahydroquinone	3	30	1.5	2.5	20	2,3,6-Trimethyl-1,4-di-hydroanthraquinone (IX)	2	229–230	81.86, 80.90	6.49, 6.40	80.92	6.39

1. Preparation of 6-methylnaphthoquinone

(I). For this experiment 50 g of p-benzoquinone, 32 g of isoprene and 150 ml of acetic acid were taken. The reaction mixture was kept at room temperature for two days and then diluted with 150 ml of water and refluxed for $1\frac{1}{2}$ hours. 300 ml of acetic acid was then added and the 6-methyl-5,8-dihydronaph-thohydroquinone formed was oxidized with chromic acid (105 g of chromium trioxide in 105 ml of water), with stirring. The oxidizing agent was added at such a rate that the temperature of the reaction mixture did not exceed 70-75°. After the addition of all the oxidizing agent, the reaction mixture was heated at 70-75° for 1 hour after which it was cooled to room temperature and diluted with 2 volumes of water. The quinone (I) was separated, washed with water a few times and dried. Yield 52 g (65%, calculated on the p-benzoquinone). M.p. 90° (from petroleum ether). According to the literature [3]: m.p. 92°.

2. Preparation of 5-methylnaphthoquinone

(II). For this experiment 50 g of p-benzoquinone, 66 g of piperylene, 66 ml of acetic acid and 2-3 drops of aniline were taken. The reaction mixture was heated at 50° for $1\frac{1}{2}$ hours. Excess piperylene was distilled off in vacuo, 100 ml of acetic acid addes and the resulting solution was refluxed for 3 hours. The 5-methyl-5,8-dihydronaphthoquinone so obtained was oxidized with chromic acid (105 g of chromium trioxide in 105 ml of water) under the conditions of Experiment 1. Yield 55 g (70%, calculated on the p-benzoquinone). M.p. 114-117° (from petroleum ether): According to the literature [3] m.p. 122.5-123°.

3. Preparation of 6,7-dimethylnaphtho-

quinone (III). In this experiment, 40 g of 6,7-di-methyl-5,8-dihydronaphthohydroquinone [2]was dis-solved in 300 ml of acetic acid and oxidized with chromic acid (72 g of chromium trioxide in 72 ml of water). Oxidation of the hydroquinone and isolation of the quinone was carried out under the conditions of Experiment 1. Yield 34 g (75%), m.p. 116-117° (from alcohol). According to the litera-ture [4]: m.p. 118-119.

4. Preparation of 2,3-dichloronaphthoquinone

(IV). A mixture of 2.5 g of 2,3-dichloro-p-benzo-quinone, 1.5 g of butadiene and 20 ml of acetic acid was kept at room temperature for 2 days and then refluxed for 2 hours to isomerize the adduct of 2,3-dichloro-p-benzoquinone and butadiene. Chromic acid solution (3.5 g of chromium trioxide

in 3.5 ml of water) was used for the oxidation. Oxidation and isolation of the quinone (IV) was carried out as in Experiment 1. Yield 2.5 g (77%, calculated on the 2,3-dichloro-p-benzoquinone). M.p. 190-192°. According to the literature [5]; m.p. 193°.

5. Preparation of 6-methyl-1,4-dihydro-1,4-endoethyleneanthraquinone (V).   To a solution of 4.4 g of 6-methyl-1,4-dihydro-1,4-endoethyleneanthrahydroquinone [2] in dioxan, heated to 50°, the oxidizing agent prepared from 2.2 g of potassium bromate, 3.5 ml of 1 N sulfuric acid and 25 ml of water, was added gradually up to the distinct appearance of color in the solution: the reaction was accompanied by the separation of yellow crystals of 6-methyl-1,4-dihydro-1,4-endoethyleneanthraquinone (V). The reaction mixture was cooled, the crystalline quinone (V) separated, washed a few times with water and dried. The yield of quinone (V) and its melting point are given in the table.

6. Preparation of 6,7-dimethyl-1,4-dihydro-1,4-endoethyleneanthraquinone (VI).   15 g of 6,7-dimethyl-naphthoquinone (III) and 30 ml of cyclohexadiene were used in this experiment and the reaction mixture was heated for 2 hours at 60°. The solution was kept overnight in a fume cupboard. The crystalline adduct of 6,7-dimethylnaphthoquinone and cyclohexadiene that separated was recrystallized from alcohol. Yield 14.4 g (60%, calculated on the quinone). M.P. 161° (from alcohol).

Found %   C 81.25, 81.28; H 6.70, 6.80. $C_{18}H_{18}O_2$. Calculated % C 81.17; H 6.80.

In order to isomerize the adduct obtained to 6,7-dimethyl-1,4-dihydro-1,4-endoethyleneanthrahydroquinone, it was refluxed for 2 hours in 50 ml of acetic acid. 6,7-Dimethyl-1,4-dihydro-1,4-endoethylene-anthrahydroquinone [2], which is a   white, crystalline material, rapidly darkening in air, was dissolved in dioxan and oxidized with potassium bromate. Oxidation and isolation of the quinone (VI) was carried out as in Experiment 5. The composition of the oxidizing mixture, yield and melting point of quinone (VI) are given in the table.

SUMMARY

1. 5-Methyl- and 6-methylnaphthoquinone and 2,3-dichloronaphthoquinone have been prepared from p-benzoquinone, 2,3-dichloro-p-benzoquinone and dienic hydrocarbons. 6,7-Dimethylnaphthoquinone has been prepared by oxidation of 6,7-dimethyl-5,8-dihydronaphthohydroquinone.

2.   The following compounds have been prepared by oxidation of the corresponding hydroquinones with potassium bromate in an acidic medium: 6-methyl-1,4-dihydro-1,4-endoethyleneanthraquinone, 6,7-dimethyl-1,4-dihydro-1,4-endoethyleneanthraquinone, 6,7-dimethyl-5,8-dihydroanthraquinone, 2,3,5-trimethyl-1,4-di-hydroanthraquinone and 2,3,6-trimethyl-1,4-dihydroanthraquinone.

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REACTIONS OF HYDRAZINE DERIVATIVES

XXI. 1-THIOCARBOXYPYRAZOLINES AND THEIR DERIVATIVES

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In recent years derivatives of thiourea have found application as antimicrobial substances [1], rodenticides [2], etc. Salts of dithiocarbamic acids are widely used in analytical chemistry for the separation and quantitative determination of some cations [3].

We have synthesized some phenylthioureas of the pyrazoline series, namely the anilides of 1-pyrazoline-thiocarbonic acids (I-VIII, see Table 1). The method consisted in treatment of pyrazolines, not substituted at the nitrogen (in the 1-position), with phenyl isothiocyanate.
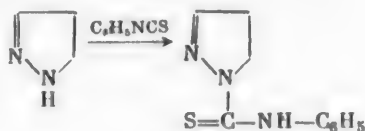
TABLE 1

Anilides of 1-Pyrazolinethiocarbonic Acids

Sub-stance No.	1-(N-Phenylthiocarba-mido)-pyrazolines	Empirical formula	Melting point	% N	
				found	calculated
(I)	(Without substituents)	$C_{10}H_{11}N_3S$	79—80°	20.54, 20.67	20.48
(II)	5-Methyl	$C_{11}H_{13}N_3S$	101—102	18.73, 18.99	19.16
(III)	3,5,5-Trimethyl	$C_{13}H_{17}N_3S$	98—99*	17.39, 17.41	16.99
(IV)	4-Ethyl-5-propyl	$C_{15}H_{21}N_3S$	54.5—55	15.39, 15.57	15.25
(V)	3-Methyl-5-5-penta-methylene	$C_{16}H_{21}N_3S$	152.5—153	14.69, 14.74	14.62**
(VI)	3-Methyl-5-phenyl	$C_{17}H_{17}N_3S$	134—135	14.27, 14.39	14.22
(VII)	3,5-Diphenyl	$C_{22}H_{19}N_3S$	173—175	11.55, 11.99	11.82***
(VIII)	3-Methyl-5-α-furyl	$C_{15}H_{15}ON_3S$	133—134	14.62, 14.68	14.73

*Literature data [11]: m.p. 104°.

**Found %: S 10.93, 11.24. Calculated %: S 11.15.

***Found % S 9.09, 9.14. Calculated %: S 9.00.

The action of carbon disulfide on pyrazolines led to 1-pyrazolinedithiocarbonic acids (in the form of the sodium salts). These salts have good solubility in water, crystallize nicely, and are stable when stored dry. Their aqueous solutions give an alkaline reaction; acidification results in breakdown since the corresponding dithiocarbonic acids are unstable.
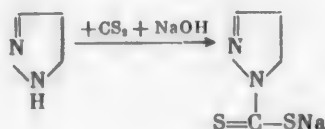
0.2% aqueous solutions of sodium pyrazolinedithiocarbonates can be kept for 2-3 days without decomposition; at pH 5-5.5 the half life of the substance is up to 30 minutes, which is adequate for analytical use (it is not desirable to work in more-acid media).

In a preliminary communication [4] it has already been noted that solutions of sodium pyrazolinedithiocarbonates have characteristic light-absorption maxima in the 290-310 mμ region. At pH 14 they precipitate metals of the platinum group, Co^{3+}, Ni^{2+}, Cu, Ag, Cd, Hg^{2+}, Tl^{1+}, Tl^{3+}, and Pb. At pH 9 all of the above-mentioned cations are brought down, in addition to Mn^{2+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Zn, In, Sn^{2+}, Sb^{III} and Te^{IV}. In still more-acidic media (pH 5) the following are also precipitated: V^{IV}, V^{V}, Cr^{3+}, Mo^{VI}, U^{VI}, Ga^{3+}, As^{III}, Se^{IV} and Sn^{VI}. Elements that are not precipitated at any of the above pH values are the alkali, alkaline earth and rare earth elements, Ti^{III}, Ti^{IV}, Zr, Th, U^{IV}, W, Al, Ge, Se^{VI}, As^{V} Sb^{V}, and Te^{VI}. (Experimental work by V. M. Byr'ko.).

TABLE 2

Pyrazolinedithiocarbonates

Substance No.	Sodium salts of 1-dithio-carboxy-pyrazolines	Yield (%)	Empirical formula	% N	
				found	calcu-lated
(IX)	5-Methyl	58.5	$C_5H_7N_2S_2Na$	15.30, 15.65	15.55
(X)	3,5,5-Trimethyl	88	$C_7H_{11}N_2S_2Na$	17.15, 13.31	13.32
(XI)	5-Methyl-3,5-diethyl	44	$C_8H_{13}N_2S_2Na$	12.44, 12.57	12.49
(XII)	4-Isopropyl-5-isobutyl	38	$C_{11}H_{19}N_2S_2Na$	10.64, 10.72	10.52
(XIII)	3-Methyl-5-α-furyl	85	$C_9H_9N_2S_2Na$	11.11, 11.23	11.37
(XIV)	3-Methyl-5,5-pentamethylene	61	$C_{10}H_{15}N_2S_2Na$	11.14, 11.17	11.19
(XV)	3,5-Diphenyl	69	$C_{16}H_{13}N_2S_2Na$	8.73, 8.97	8.74
(XVI)	3-Methyl-5-phenyl	55	$C_{11}H_{10}N_2S_2Na$	12.57, 12.63	12.44
(XVII)	4,4-Dimethyl-5-isopropyl	34	$C_9H_{15}N_2S_2Na$	12.18, 12.23	12.27
(XVIII)	3,4-Tetramethylene-5,5-pentamethylene	63	$C_{13}H_{19}N_2S_2Na$	9.73, 9.89	9.65

The prepared pyrazolinedithiocarbonates (IX-XVIII, Table 2) break down at below their melting points; for their characterization we therefore prepared the β-cyanoethyl ethers by treatment with acrylonitrile in an aqueous medium. The new derivatives melt sharply.
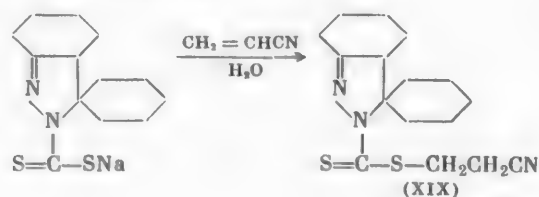
In one of our preceding papers [5] we showed that phenylhydrazine does not form a pyridazine ring on heating with acetopropyl alcohol. It was found that hydrazine hydrate reacts analogously to give an azine ring with acetopropyl alcohol. But if the hydroxyl group is replaced beforehand by chlorine, then the resulting methyl-γ-chloropropyl ketone readily reacts with hydrazine hydrate to form 3-methyl-1,4,5,6-tetrahydropyridazine (XX). The properties of (XX) are very similar to those of pyrazolines. It gives off nitrogen on treatment with strong oxidants; with carbon disulfide it forms 1-dithiocarboxytetrahydropyridazine (XXI), and with phenylisothiocyanate it gives the corresponding thiourea (XXII).
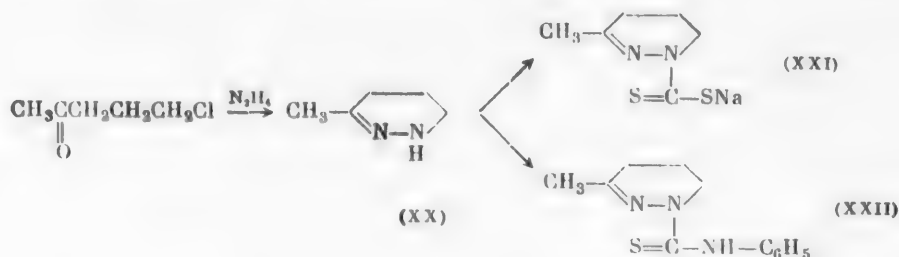
According to R. Ya. Levina and co-workers [6], tetrahydropyridazines lose nitrogen under the conditions of the N. M. Kizhner reaction to form cyclobutanic hydrocarbons. We heated our tetrahydropyridazine with sodium, potassium or lithium hydroxides, in the presence or absence of water, without solvents or in triethyleneglycol, but at below 250°. The main body of substance was recovered unchanged, but at a higher temperature (in an autoclave) complete resinification was observed.

A study of the action of the prepared substances on microorganisms revealed that in 1:1000 dilution, phenylureas of the pyrazoline series (Table 1) have no action on Staphylococcus aureus, hemolytic streptococci, Bacillus diphtheriae, Bacillus dysenteriae, Bacillus cyanogenus, Bacterium coli, Bacillus typhosum, and Bacillus sporogenes. The bacillus Proteus vulgaris was also unaffected. Compound (V) is an exception: in 1:4000 dilution it inhibits growth of Bacillus diphtheriae, and in 1:2000 dilution it inhibits the growth of Bacillus cyanogenus. The maximum activity towards the bacillus of human tuberculosis was exhibited by compound (I), which suppresses the growth of this microorganism in dilutions of 1:16000 to 1:32000. The same compound suppresses the growth of pathogenic fungi when in dilution of 1:1000 to 1:4000. Compound (II) is slightly less active, but the remaining compounds suppress the growth of the bacillus of human tuberculosis in dilution of 1:500 to 1:2000, and at these dilutions they are substantially inactive towards all of the remaining microorganisms.

A strong fungistatic action might have been expected to be exerted by the sodium salts of 1-dithiocarboxypyrazolines (Table 2), in analogy with the behavior of other dithiocarbamates [7]. Compounds (IX-XVIII), also (XXI), actually possess antimicrobial action, mainly towards streptococci and Bacillus diphtheriae, but in low dilution (from 1:1000 to 1:8000). 5,5-Disubstituted derivatives (X, XI, XIV, XVIII) manifested fungicidal action, but again in low dilution (1:2000 to 1:8000). The β-cyanoethyl ether (XIX) has substantially no antimicrobial action; the analogous ether prepared from (XXI) inhibits the growth of the bacilli of human tuberculosis in dilution of 1:1000 to 1:2000. None of the prepared compounds exerted single-dose or cumulative toxic action when administered in nutriment to rats in doses of up to 50 mg per 1 kg of body weight (the doses were repeated 3 times). •

EXPERIMENTAL

Anilides of pyrazolinethiocarbonic acids (I-VIII) were prepared by the action of phenylisothiocyanate in benzene on the corresponding pyrazolines. Yields were nearly quantitative. All of the compounds prepared by this method were recrystallized from alcohol. The constants and data for elemental analysis are set forth in Table 1.

•Tests on rats were carried out by N. M. Dukel'skaya (Soil Biology Department of Moscow State University).

3-Methyl-1,4,5,6-tetrahydropyridazine (XX). To 48.8 g methyl γ-chloropropyl ketone, dissolved in 100 ml alcohol and put into a 500-ml flask fitted with a small Dimroth condenser, was added 20.8 g 96% hydrazine hydrate. An extremely violent reaction ensued. After the violent boiling-up of the mixture had ceased, the mixture was boiled for 1.5 hr and the alcohol was completely distilled off in the vacuum of a water-jet pump. The resulting hydrochloride was decomposed by addition of 88 g barium oxide and the base was twice-distilled in vacuo. Yield 38.4 g (98%) of 3-methyl-1,4,5,6-tetrahydropyridazine (XX).

B.p. 78° (30 mm), n_D^{20} 1.4950, d_4^{20} 0.9714, MR_D 29.46; calc. 29.34. •

Found %: N 28.48, 28.48. $C_5H_{10}N_2$. Calculated %: N 28.54.

The phenylthiourea derivative (XXII) had m.p. 124° (from alcohol).

Found %: N 18.19, 18.25. $C_{12}H_{15}N_3S$. Calculated %: N 18.01.

Sodium salt of 1-dithiocarboxy-3-methyl-1,4,5,6-tetrahydropyridazine (XXI). To a solution of 9.4 g 3-methyltetrahydropyridazine (XX) in 20 ml alcohol was added 8 ml 35% aqueous sodium hydroxide followed by 9 g carbon disulfide. The mixture was stirred vigorously for 2 hr and then cooled; the sodium salt (XXI) came down in nearly quantitative yield. It was purified by recrystallization from acetone.

Found %: N 15.48, 15.57. $C_5H_7N_2S_2Na$. Calculated %: N 15.37.

Sodium salt of 1-dithiocarboxy-3,5,5-trimethylpyrazoline (X). To a solution of 0.05 mole of freshly distilled 3,5,5-trimethylpyrazoline [8] in 15 ml benzene was added 1.5 ml 35% aqueous solution of sodium hydroxide, followed by 4.6 g carbon disulfide (with energetic stirring). The crystals that came down on cooling were recrystallized from aqueous acetone. Yield 9.25 g (88%) of sodium salt (X). The melting point was not sharp (decomposition above 200°). A similar procedure was followed for preparation of (II-VIII). (IX) was purified by precipitation with benzene from alcohol, (XIII and XVIII) by precipitation with ether from methanol, (XVI) by precipitation with ether from ethanol, and the remaining substances by precipitation with ether from acetone. Yields (after recrystallization) and analyses are set forth in Table 2.

β-Cyanoethyl ether or 1-dithiocarboxy-3,5,5-trimethylpyrazoline. To a 20% aqueous solution containing 4.85 g sodium salt (X) was added 1.6 g acrylonitrile. The mixture was stirred 2 hr at room temperature. The precipitated crystals were filtered off and recrystallized from alcohol to give 3.5 g (62%) β-cyanoethyl ether, with m.p. 165-165.5°.

Found %: N 17.15, 17.19; S 26.51, 26.86. $C_{10}H_{15}N_3S_2$. Calculated %: N 17.48; S 26.67.

In similar fashion the sodium salt (XVIII) gave a 70% yield of the β-cyanoethyl ether of 1-dithiocarboxy-3,4-tetramethylene-5,5-pentamethylenepyrazoline (XIX), with m.p. 176° (from alcohol).

Found %: N 12.99, 13.05. $C_{16}H_{23}N_3S_2$. Calculated %: N 13.09.

The cyanoethyl ether was prepared from (IX) in 46% yield; m.p. 158° (from alcohol).

Found %: N 19.43, 19.59. $C_8H_{11}N_3S_2$. Calculated %: N 19.70.

The cyanoethyl ether of (XIII) was synthesized in 57% yield; m.p. 97-98° (from alcohol).

Found %: N 14.96, 15.20; S 23.00, 23.19. $C_{12}H_{13}ON_3S_2$. Calculated %: N 15.15; S 23.11.

In similar fashion the sodium salt of 1-dithiocarboxy-3-methyltetrahydropyridazine (XXI) was converted to the β-cyanoethyl ether in 95% yield; m.p. 102° (from anhydrous alcohol).

Found %: N 18.68, 18.53. $C_9H_{13}N_3S_2$. Calculated %: N 18.48.

L. S. Ignatenko carried out the elemental analyses of the prepared compounds, using the procedure of P. N. Fedoseev [9] which was developed for poorly stable or difficultly combustible substances. The usual methods for analysis of pyrazoline derivatives give very variable results [10].

• The refraction for the 2 N atoms in the tetrahydropyridazine is assumed to be 5.871 (as in pyrazolines).

SUMMARY

A series of sodium salts, β-cyanoethyl ethers and anilides of dithiocarbonic acids of the pyrazoline family were synthesized. Their action on microorganisms was investigated.

Pyrazolinedithiocarbonates are found to form inner-complex compounds with a number of cations of metals, and this property may be of interest for analytical purposes.

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THE ISOMERIZATION OF POLYMETHYLENE HYDROCARBONS UNDER THE INFLUENCE OF ALUMINUM CHLORIDE

XXII. THE ISOMERIZATION OF DICYCLOPENTYLMETHANE

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In one of our preceding papers [1] we described the isomerization of dicyclopentyl, under the influence of aluminum chloride, to trans-decahydronaphthalene. The temperature in the range of 0 to 50° does not influence the character of the product of isomerization. At higher temperatures products of cracking are formed and isomerization is more far-reaching.

In the present work we studied the behavior of dicyclopentylmethane (a hydrocarbon whose properties suggest that it may be present in the kerosine fraction of petroleum) on interaction with aluminum chloride, and we clarified the effect of the methylene group, linking the two five-membered rings, on the direction of isomerization. The experimental results of the present work have established that aluminum chloride here has an effect similar to that in the case of dicyclopentyl, the dicyclopentylmethane undergoing skeletal isomerization with formation of trans-β-methyldecahydronaphthalene. At 23-27° isomerization goes to the extent of about 96-98%; at 0° it goes in the same direction but to a lesser extent. Lowering of the temperature to -5° retards the reaction to such an extent that a product of isomerization cannot be detected. The presence of β-methyldecahydronaphthalene was demonstrated by the method of catalytic dehydrogenation and confirmed by the Raman spectrum. Dehydrogenation yielded β-methylnaphthalene, which was identified as the picrate. Under the same conditions dicyclopentylmethane underwent hydrogenolysis, as would be expected in view of its structure. The spectrum of the product of isomerization of dicylopentylmethane contained lines characteristic of trans-β-methyldecahydronaphthalene.

The data obtained in the present work have consequently shown that the methylene located between the two five-membered rings of dicyclopentylmethane has no appreciable influence on the direction of isomerization.

The following explanation of the mechanism of isomerization of dicyclopentylmethane to trans-β-methyl-decahydronaphthalene may be suggested: Since both of the five-membered rings of the dicyclopentylmethane system are equivalent in relation to the methyl group, we should expect simultaneous breakage of both rings under the action of aluminum chloride. Two possibilities could then arise in connection with the formation of fresh bonds in the isomerizing molecule: either formation of spiro-(5,5)-undecane ,

which (as we showed previously [2]) is improbable, or direct formation of the condensed system of methyldeca-hydronaphalene
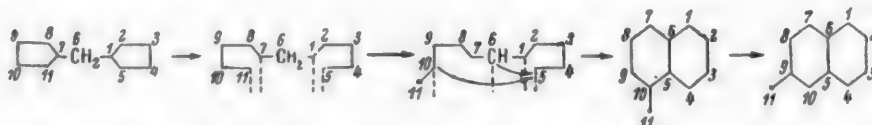
In spite of the symmetry of the dicyclopentylmethane molecule, it is entirely probable that in the instant of isomerization this symmetry is destroyed due to opening of one of the rings, and then the reaction must proceed otherwise. If we imagine, however, that rupture of the five-membered rings in dicyclopentylmethane is

a stepwise process, i.e. that rupture of one of the rings precedes rupture of the other, then cyclohexylcyclopentane could be formed and could then isomerize to trans-β -methyldecahydronaphthalene by the route previously suggested by us [3].

EXPERIMENTAL

Dicyclopentylmethane was prepared by the method of Platé and Stanko [4].
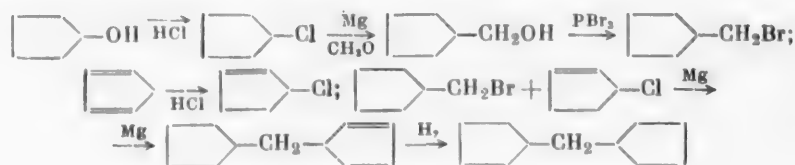
The starting substance for our work was not bromocyclopentane but chlorocyclopentane, prepared from cyclopentanol [5,6].

B.p. 113.1° at 740 mm, n_D^{20} 1.4522, d_4^{20} 1.0071, MR_D 28.00. C_5H_9Cl. Calculated 27.96.

Cyclopentylcarbinol was obtained by the reaction of chlorocyclopentane with formaldehyde in a Grignard reaction [7].

B.p. 160.5-162.5° (742.5 mm), n_D^{20} 1.4580, d_4^{20} 0.9336, MR_D 29.22. $C_6H_{10}O$. Calculated 29.22.

Literature data [4]: B.p.106-108° (82 mm), n_D^{20} 1.4575, d_4^{20} 0.9322.

Treatment of cyclopentylcarbinol with phosphorus tribomide [7] gave cyclopentylbromomethane.

B. p. 59-59.5° (20 mm), n_D^{20} 1.4874, d_4^{20} 1.3079.

Literature data [4]: b.p. 58-62° (20 mm), n_D^{20} 1.4859, d_4^{20} 1.2920.

Δ^2-Chlorocyclopentene, obtained by the action of dry, gaseous hydrogen chloride on cyclopentadiene [8] (b.p. 37° at 38 mm, n_D^{20} 1.4765) was brought into reaction with cyclopentylbromomethane and magnesium immediately after distillation. The resulting Δ^2-cyclopentenylcyclopentylmethane had the following constants:

B.p. 89° (16 mm), n_D^{20} 1.4770, d_4^{20} 0.8801, MR_D 48.16. $C_{11}H_{18}F$. Calculated 48.13.

Literature data [4]: b.p. 80.5-80.7° (11 mm), n_D^{20} 1.4778, d_4^{20} 0.8813, MR_D 48.16.

Hydrogenation of Δ^2-cyclopentenylcyclopentylmethane at room temperature and a hydrogen pressure of 100 atm. in presence of not completely lixiviated Raney alloy [9] (15% of the weight of hydrocarbon) gave dicyclopentylmethane. The latter was subjected to chromatographic adsorption on silica gel, distillation in a column (80-plate), and further chromatography on silica gel. The so-purified dicyclopentylmethane had the following constants:

B.p. 80.5° (8 mm), freezing point -74.18°, n_D^{20} 1.4677, d_4^{20} 0.8675, MR_D 48.60. $C_{11}H_{20}$. Calculated 48.60; degree of purity 99.60% •

Literature data [4]: b.p. 83.3- 83.4° (10 mm), n_D^{20} 1.46777, d_4^{20} 0.8675, MR_D 48.60.

The Raman spectrum of dicyclopentylmethane was examined. The intensity of the lines was determined visually and evaluated on an arbitrary scale.

Spectrum of dicyclopentylmethane (cm^{-1}): 229 (0); 291 (80); 406 (0); 414 (0); 776 (0); 792 (0); 808 (0); 833 (0); 843 (0); 890 (80); 943 (1); 978 (0); 1014 (12, b•;d•); 1038 (1.5; b•;d•); 1068 (3); 1085-1103 (12; b•;d•); 1144 (0.5,d•); 1165 (0); 1174 (11; b•;d•); 1187 (11; b•;d•); 1285 (4); 1296 (5, d•); 1307 (0); 1351 (10); 1390 (0); 1443 (80).

•This constant was determined by the procedure of [10].

•• d = diffuse. b = broad.

Dicyclopentylmethane was passed over a platinum catalyst containing iron (19.6% Pt and 2% Fe) under conditions of dehydrogenation catalysis, i.e. at 300-310°, at a low rate in a hydrogen atmosphere. After the first pass the catalyzate had n_D^{20} 1.4658, d_4^{20} 0.8603; after the second pass it had n_D^{20} 1.4630, d_4^{20} 0.8535. These changes indicated hydrogenolysis of dicyclopentylmethane. Isomerization of dicyclopentylmethane was performed in the apparatus used in previous work [11]. In all of the experiments the aluminum chloride/hydrocarbon molar ratio was constant at 1:3. The hydrocarbon was distilled immediately before the reaction; the aluminum chloride was sublimed. The reaction mixture was stirred for 15-18 hours. No gaseous products were formed.

Experiment 1 was performed at -5 to -8°. Aluminum chloride was added to the hydrocarbon which had previously been cooled to the low temperature. No change of temperature was observed. After completion of the reaction, the hydrocarbon layer was decanted off from the aluminum chloride, washed, dried and distilled over sodium. Its constants (Table 1) and spectrum were substantially the same as those of the original hydrocarbon:

231 (0); 291 (80); 397 (0); 406 (0); 414 (0); 496 (0); 718 (0); 735 (0); 746 (0); 776 (0); 792 (0); 808 (0); 831 (0); 843 (0); 890 (80); 912 (0); 943 (0.5); 1014 (12; b•,d•); 1038 (7; d•); 1068 (7; d•); 1085 (7; d•); 1098 (12; b•,d•); 1133 (0); 1144(0); 1165 (0); 1174 (5); 1187 (5; d•); 1285 (3; d•); 1296 (3); 1304 (3; d•); 1317 (0); 1352 (10); 1390 (0.5); 1443 (80); 1477 (2).

All of the frequencies of the spectrum of the product were the same as those of the spectrum of dicyclopentylmethane, but the strongest line of the spectrum [12] of trans-β-methyldecahydronaphthalene (755 cm^{-1}) was absent.

Experiment II was performed at 0°. There was again no change of temperature when aluminum chloride was added to the cooled hydrocarbon. After appropriate purification the reaction product had the constants given in the table, in which are also set forth the constants of the original hydrocarbon and methyldecahydronapthalene.

TABLE 1

Hydrocarbons and products of their reactions		Boiling point(pressure in mm)	n_D^{20}	d_4^{20}
Original dicyclopentylmethane		206.5 − 208° (746)	1.4677	0.8675
Reaction product	Expt. I	206 (750)	1.4660	0.8666
	Expt. II	208 − 210 (755)	1.4672	0.8669
	Expt. III	206.5 (753)	1.4701	0.8697
Trans-β-methyldecahydronaphthalene [12]		76 (12)	1.4698	0.8693
Cis-β-methyldecahydronaphthalene [12]		84 (12)	1.4751	0.8846

One portion of the reaction product was subjected to dehydrogenation, and another was examined for its Raman spectrum. Dehydrogenation was performed over the same catalyst and under the same conditions as for the dehydrogenation of the original dicyclopentylmethane. The presence of β-methylnaphthalene in the catalyzate was confirmed by formation of the picrate with m.p. 115.5-116° (from alcohol).

According to the literature[14], β-methylnaphthalene picrate melts at 116°, and α-methylnaphthalene picrate at 141°.

Spectrum of reaction product:

233 (0); 291 (0); 340 (0); 373 (5); 408 (2); 442 (0.5); 466 (0.5); 502 (4); 753 (6); 769 (0); 792 (0); 833 (0); 853 (2) 893 (10; b•); 1017 (2; d•); 1044 (4); 1057 (0.5); 1074 (2; d•); 1104 (2; d•); 1144 (0.5; d•); 1165 (4); 1187 (0;d•); 1203 (1.5; d•); 1253 (3; b•,d•); 1296 (0; b•,d•); 1347 (4); 1354 (4); 1443 (20; b•).

• d = diffuse,   b = broad.

The following lines were found in the spectrum in addition to those of dicyclopentylmethane: 373 (5); 502 (4); 753 (6); 853 (2); 1044 (4); 1074 (2;d•), characteristic of trans-β-methyldecahydronaphthalene.

Experiment III was performed at 23°. Addition of aluminum chloride to dicyclopentylmethane caused the temperature to rise to 27°, after which it fell to the original value. The product was purified and distilled (see table for constants), and a portion was dehydrogenated. The first pass gave a catalyzate with n_D^{20} 1.5350; after the second pass the product had $n^{20}D$ 1.5405, after the third pass it had n_D^{20} 1.5630, and after the fourth pass n_D^{20} 1.5910 (the product of isomerization had n_D^{20} 1.4701; β-methylnaphthalene has n_D^{40} 1.6019 [13]).

The picrate obtained from the catalyzate melted (after recrystallization from alcohol) at 115.5-116°. A mixture of the prepared picrate with β-methylnaphthalene picrate melted at 115.5-116°, i.e. did not exhibit a depression. A second portion of the product of isomerization of dicyclopentylmethane was subjected to spectral analysis.

Spectrum of the prepared product:

284 (3); 330 (0); 347 (0); 371 (8); 406 (3); 440 (0.5; b•,d•); 464 (0.5; b•,d•); 496 (7.5, d•); 530 (0.5); 753 (7); 769 (0); 792 (0); 808 (0); 831 (0); 850 (3); 890 (2; b•,d•); 978 (0.5 b•,d•); 1014 (0); 1038 (5); 1057 (2); 1073 (0.5; f ••); 1104 (0.5; d•); 1144 (0); 1160 (5); 1196 (0.5;b•,d•); 1219 (0); 1250 (3); 1263 (0);1347 (1.5; d•); 1354 (4); 1443 (10); 1460 (1; d•).

All of the most characteristic lines of trans-β-methyldecahydronaphthalene [3] are present in this spectrum: 371 (8); 753 (7); 850 (3); 1038 (5); 1073 (0.5, f ••). The presence of an insignificant quantity (about 2-4%) of unchanged dicyclopentylmethane is also indicated [lines 284 (3); 890 (2; b•, d•)]. In this spectrum the lines of trans-β-methyldecahydronaphthalene were more intense than in the spectrum of the reaction product of experiment II.

SUMMARY

1. The product of isomerization of dicyclopentylmethane in presence of aluminum chloride is trans-β-methyldecahydronaphthalene.

2. The temperature in the range of 0 to 27° does not influence the character of the isomerization product.

3. The yield of β-methyldecahydronaphthalene at 23-27° is about 96-98%.

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• d = diffuse   b = broad.
••
    f = line located against a background of considerable intensity.
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THE ALKYLATION OF NAPHTHALENE WITH THE MOLECULAR COMPOUND OF ETHYL ALCOHOL AND BORON FLUORIDE UNDER PRESSURE

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As was shown in the preceding publications [1,2], naphthalene is relatively easily alkylated by molecular compounds of alcohols with boron fluoride at the ordinary pressure and at a temperature of 165-170°. Under these conditions a mixture of α- and β-alkylnaphthalenes and dialkylnaphthalenes is obtained. The content of α-isomer in the monosubstituted products obtained under these conditions is usually 45-50%. In later work [3,4] we found that the main products are β-isomers if alkylation with molecular compounds is performed at the same temperature but at a pressure of 20-30 atm. Thus, the alkylation of naphthalene with the molecular compound of isoamyl alcohol and BF_3 under these conditions gave mainly β-tert-amylnaphthalene [3]. Similar behavior was noted in reactions with other alcohols.

It is known that alkylation with ethyl alcohol goes with much less facility than with other alcohols. By means of our reaction, however, naphthalene can be alkylated with ethyl alcohol to give a mixture of α-and β-methylnaphthalenes. The β-ethylnaphthalene content is 85-90%. The yield of monoethylnaphthalenes, calculated on the original naphthalene, is 58-63%.

EXPERIMENTAL

Alkylation of naphthalene with ethyl alcohol was performed in a 0.5-liter steel autoclave fitted with mechanical stirrer and electrical heater. The reaction was run in two steps. The previously prepared molecular compound of ethyl alcohol and boron fluoride was charged into the autoclave together with naphthalene in the ratio of 2.5-3 moles of the former to 1 mole of the latter. No solvent was employed. The temperature was gradually raised to 165°, at which point the pressure reached 25-27 atm. Heating was immediately cut off but the temperature continued to rise to 170° before gradually falling to room temperature. After cooling, the contents of the vessel were poured into water, worked up in the usual manner and dried over calcium chloride. Distillation was then carried out, first over metallic sodium and then in a vacuum column (48-50 theoretical plates). A compound with the following constants was collected:

B.p. 258°, 76.4°*(0.7 mm), d_4^{20} 0.9928, n_D^{20} 1.6003. M 156.2, 156; setting point − 7.8°.

According to the literature [5], β-ethylnaphthalene has b.p. 258°, d_4^{20} 0.992, n_D^{20} 1.5999, setting point -7°.

SUMMARY

β-Ethylnaphthalene was synthesized by alkylation of naphthalene with ethyl alcohol in presence of boron fluoride.

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*As in original.

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ALKYLATION OF BENZENE WITH THE MOLECULAR COMPOUNDS
OF ALCOHOLS AND BORON FLUORIDE UNDER PRESSURE

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In preceding work [1-4] we showed that naphthalene and biphenyl are relatively easily alkylated by the molecular compounds of alcohols and boron trifluoride at elevated temperature. The main products are mono-alkylnaphthalenes and monoalkylbiphenyls. But if the reaction is run at a pressure of 20-30 atm., the proportion of dialkylated hydrocarbons increases. Alkylation of biphenyl with molecular compounds under pressure gives predominantly para-substituted alkylbiphenyls. On applying this reaction to toluene, we were able to show that the reaction takes a similar course, the alcohol radical entering mainly in the para-position to the methyl [5].

At the present time a number of monoalkylbenzenes, such as ethylbenzene, isopropylbenzene and isobutyl-benzene, are extensively used in the production of valuable organic raw materials for plastic masses and synthetic fibers. 1,4-Dialkylbenzenes are oxidized to terephthalic acid — the starting substance for "Terylene." In view of the importance of alkylbenzenes, we applied our alkylation technique to benzene.

In this work we reacted benzene with molecular compounds of alcohols (ethyl, n-propyl, isopropyl, iso-and n-butyl and isoamyl) and boron fluoride. The reaction was performed in an autoclave at 200-230° and 75-120 atm. Mixtures of mono- and dialkylbenzenes were obtained in yields of 60-90% (calculated on the original benzene). Alkylation of benzene with ethyl alcohol gave a mixture of monoethylbenzene and diethylbenzenes in total yield of 60-64%; the ethylbenzene made up about 65-70% of the mixture (calculated on the total yield of ethylbenzenes). The remainder was a mixture of diethylbenzenes with very little triethylbenzenes. The Raman spectrum indicated the presence of 75-80% of 1,4-isomer in the mixture of diethylbenzenes; the remainder was a mixture of 1,3- and 1,2-isomers.

Alkylation of benzene with n-propyl and isopropyl alcohols gave the same product — isopropylbenzene. In previous work [3,4] we showed that alkylation of naphthalene and biphenyl with normal alcohols at atmospheric pressure gave alkylnaphthalenes and alkylbiphenyls with normal radicals. These reactions evidently involve a condensation process and not alkylation with intermediate olefins. Reaction at a pressure of 75-120 atm., however, mainly involves alkylation with olefins in accordance with the Markovnikov rule. A similar phenomenon was observed in alkylation of benzene with n-butyl and isobutyl alcohols: only isobutylbenzene was formed. The isopropylbenzenes and isobutylbenzenes are obtained in good yields. Alkylation of benzene with n-propyl al-cohol gave 78-84% of isopropylbenzenes; in the reaction with isopropyl alcohol the yield of isopropylbenzenes was 84% (calculated on the benzene brought into reaction). It was found that the yield of diisopropylbenzenes depends on the quantities of alcohol introduced into the reaction: with an alcohol/benzene ratio of 1:1.25 the yield of diisopropylbenzenes did not exceed 15-18%; with ratios of 1:1.5 or 1:1.75 the yields of dialkylbenzenes rose to 40-50% (calculated on the total quantity of alkylbenzenes). The Raman spectra indicated that 75-80% of the dialkylbenzenes were 1,4-dialkyl derivatives. Alkylation of benzene with n-butyl alcohol gave isobutyl-benzenes in 92% yield; the yield of monoisobutylbenzene was 70-71% As in the case of propyl alcohols, an increase in the amount of reacting alcohol leads to higher yields of diisobutylbenzenes.

Alkylation of benzene with isoamyl alcohol gave isoamylbenzenes in total yield of 90-93% The yield of mono- and diisoamylbenzenes depends on the ratio of benzene to original alcohol ; with a 1:1 ratio the main product is monoisoamylbenzene (80-82% of the total mixture). Among the diisoamylbenzenes the main product is the 1,4-isomer. Isoamylbenzenes possess a pleasant, fruity odor.

Alkylation of Benzene with Molecular Compounds of Alcohols with BF₃

No.	Name	Alcohol (in g)	Time (hr)	Temperature (pressure in atm.)	Compounds obtained	Boiling point found	Boiling point literature data	n^{20}_D found	n^{20}_D literature data	d^{20}_4 found	d^{20}_4 literature data	Yield (in %)
1	134	Ethyl 158	3	210°(115)	Ethylbenzene	134°	136.18°[6]	1.4938	1.4958[6]	0.8651	0.8670[6]	48
					Diethylbenzene	181.8	183.75[7]	1.4950	—	0.8623	—	16
					1,4-Diethylbenzene	—	183.75[7]	—	1.4958[7]	—	0.8619[7]	—
2	137	n-Propyl, 177	3	210(98)	Isopropylbenzene	151.6	152.39	1.4903	1.4914	0.8614	0.8608	67
					Diisopropylbenzene	208—209	—	1.4870	—	0.8558	—	19
					1,4-Diisopropylbenzene	92 (2—3 мм)	210.38[6]	—	1.4898[6]	—	0.8567[6]	—
3	137	Isopropyl, 177	2	208(100)	Isopropylbenzene	152.1	152.39	1.4907	1.4914	0.8611	0.8618	74
					Diisopropylbenzene	208—209	—	1.4870	—	0.8558	—	10
					1,4-Diisopropylbenzene	92 (2—3 мм) 210.38	—	—	1.4898[6]	—	0.8567[6]	—
4	117	n-Butyl, 220	3	215(105)	Isobutylbenzene	172.5—172.9	172.76[8]	1.4869	1.4864	0.8537	0.8532	70
					Diisobutylbenzene	241, 94 (2 мм)	243[9]	1.4847	1.4834	0.8461	0.8456[9]	22
					1,4-Diisobutylbenzene	—	—	—	—	—	—	—
5	117	Isobutyl, 220	2.5	205—215 (95—100)	Isobutylbenzene	172.85, 241,	172.76[8]	1.4880	1.4864	0.8541	0.8532[8]	60
					Diisobutylbenzene	90 (1.5 мм)	—	1.4847	1.4834	0.8458	0.8456	20
					1,4-Diisobutylbenzene	—	243[3]	—	—	—	—	—
6	117	Isoamyl, 198	2.5	210(78)	Isoamylbenzene	191.7—192	—	1.4866	—	0.8590	—	81
					Diisoamylbenzene	257,	—	1.4837	—	0.8488	—	12
					1,4-Di-tert-amyl-benzene	101 (2 мм) —	260[10]	—	1.4841	—	0.8491[10]	—

The structures of the prepared compounds were confirmed by analyses by infrared spectroscopy. *

In previous work it was found that the iso radical is converted into a tertiary radical during alkylation of naphthalene and biphenyl with isobutyl and isoamyl alcohols at atmospheric and higher pressures. Alkylation of biphenyl with isobutyl alcohol gave p-tert-butylbiphenyl with m.p. 52°; alkylation with isoamyl alcohol gave p-tert-amylbiphenyl with m.p. 46°.

In the light of these results we expected to obtain benzenes with tertiary radicals after reactions with iso-butyl and isoamyl alcohols. These expectations were not fulfilled; the alkylbenzenes formed in these reactions had the structures $C_6H_5CH_2CH(CH_3)_2$ and $C_6H_5CH_2CH_2CH(CH_3)_2$.

The butyl- and amylbenzenes that we isolated rapidly react with bromine in carbon tetrachloride; this indicates the presence of a CH group. The Raman and infrared spectra confirmed the chemical findings.

We have so far been unable to explain why normal radicals isomerize during reaction while iso radicals remain unchanged. Further work is necessary before the problem can be solved. Alkylation with alcohols is clearly a very complex and unusual process. Alkylbenzenes with iso radicals are formed side by side with ethers containing the same radicals as in the original alcohol. Alkylation of benzene with n-propyl and n-butyl alcohols gave isopropyl and isobutylbenzenes, while secondary products were dipropyl and dibutyl ethers with normal radicals. We isolated diethyl, dipropyl, diisopropyl, dibutyl, diisobutyl and diisoamyl ethers, the yields of which in some experiments reached 60-70% (calculated on the original molecular compound of the alcohol and BF_3). The direction of the reaction is found to depend on the experimental conditions, and it can be varied as desired.

EXPERIMENTAL

Alkylations of benzene with alcohols were carried out in a 0.5-liter autoclave designed for a pressure of 500 atm. Previously prepared compounds of alcohols with BF_3, corresponding to the formula $2ROH \cdot BF_3$, were charged into the autoclave together with the benzene in the ratio of 1.5-2 moles alcohol to 1 mole benzene. By means of an electric furnace the temperature was gradually raised to 200-230° (depending upon the alcohol) and it was then held for 2-3 hr. In most of the reactions the maximum pressure was 100-120 atm. The autoclave was then cooled to room temperature, and the contents were poured into water; the mass was thoroughly washed with sodium carbonate solution and finally with water. After it had been dried over calcium chloride, the product was given a preliminary distillation from a flask with a dephlegmator; it was then carefully fractionated in a 51-52-plate column. Dialkylbenzenes that did not come over at atmospheric pressure were fractionated in a vacuum column.

Reaction conditions, yields of products and constants are set forth in the table.

SUMMARY

1. Alkylation of benzene with molecular compounds of alcohols and BF_3 under the described conditions gave mono- and dialkylbenzenes in yields depending on the proportions of reactants.

2. The main product among the dialkylbenzenes was the 1,4-isomer.

3. In alkylations at the specified pressures, the n-propyl and n-butyl radicals isomerize, whereas isobutyl and isoamyl radicals remain intact.

4. Alkylation of benzene with the alcohols named gave alkylbenzenes in good yields.

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THE SYNTHESIS OF ACETALS AND KETALS WITH THE HELP OF TETRAALKYLANES

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In connection with investigations on the synthesis of isoprenoid and polyenic compounds we had to prepare acetals and ketals of various aldehydes and ketones. It is well known that esters of orthoformic acid are the most effective acetalizing agents. Due, however, to their high price, these esters cannot be used for the production of acetals and ketals on the large scale. Our attention was therefore directed towards the easily obtainable and accessible esters of orthosilicic acid (tetraaryloxysilanes).

Helferich and Hansen [1] showed that tetraalkoxysilanes can acetalize aldehydes and ketones in an alcoholic medium (2-3 moles alcohol per mole aldehyde or ketone) in presence of hydrogen chloride. We encountered a number of difficulties on attempting to prepare some acetals and ketals by this method. In numerous experiments on the preparation of ketals of acetone, for example, we obtained them in yields of only 10-15% The main product of reaction of tetramethoxysilane with crotonaldehyde was 1,1,3-trimethoxybutane (yield 60%). The dimethylacetal of crotonaldehyde was obtained in a yield of only 12-15%.

We decided to make a more-detailed study of the reaction of tetraalkoxysilanes with aldehydes and ketones under various conditions.

We tested the following as acetalization catalysts for the reaction of acetone with tetraalkoxysilane: hydrogen chloride, concentrated sulfuric acid, p-toluenesulfonic acid, phosphoric acid, boron trifluoride etherate, and trichloroacetic acid. The best catalyst was found to be phosphoric acid, and this was therefore used in the preparation of all of the acetals and ketals.

Contrary to the existing opinion, tetraalkoxysilanes readily enter into reaction with aldehydes and ketones in presence of a small quantity of alcohol. For example, acetone diethylketal is obtained in 93% yield with the help of tetraethoxysilane by using 0.5 mole alcohol per mole of acetone. The dimethyl and diethyl acetals of acetaldehyde, propionaldehyde, butyraldehyde,isobutyraldehyde, methyl ethyl ketone, citral, etc.,were similarly obtained in very good yields; the preparation of the dimethyl- and diethylacetals of crotonaldehyde was found to require only 0.1 to 0.2 mole alcohol per mole aldehyde. This is an important factor in the preparation of low-boiling acetals and ketals since the need for only a small quantity of alcohol during the acetalization reaction means that after distillation,from the reaction mass the acetals and ketals have a low content of alcohols. The latter can be easily removed from the acetal by washing with a little water. When the resulting low-boiling acetal is heavily diluted with alcohol, its purification is a difficult problem because washing with water leads to loss of a high proportion of the acetal in the aqueous alcoholic solution. Great difficulty is also attached to removal of the alcohol by distillation since difficultly resolvable azeotropic mixtures of acetals and alcohol are usually formed. The quantity of alcohol introduced into the reaction is less critical in the preparation of high-boiling acetals (of methylheptenone, cyclohexanone, furfural, etc.) since the alcohol can be easily removed by distillation.

The proportion of alcohol used in the acetalization of crotonaldehyde is particularly important. With 0.1 to 0.2 mole alcohol per mole aldehyde, dimethyl- and diethylacetals of crotonaldehyde can be obtained in a yield of up to 80% If the alcohol proportion is higher (over 1 mole) the main reaction products are 1,1,3-trialkoxybutanes [2].It is interesting to note that acetalization of crotonaldehyde also takes place in the absence of alcohol,but the reaction is very much slower and the yield of acetal is only 47%

TABLE 1

Serial No.	Name	Boiling point (pressure in mm)	n^{20}_D	Reaction conditions				Yield (%)
				carbonyl compound: tetra-alkoxysilane: alcohol(moles): 85%H_3PO_4(in ml)	temperature	duration (hr)	method of working-up	
1	Acetaldehyde diethyl-acetal	101—103°	1.3819	1 : 1 : 0.5 : 2	35—80°	8	A	61
2	Propionaldehyde di-ethylacetal	123—125	1.3894	1 : 1 : 0.5 : 2	50—80	8	A	72
3	Butyraldehyde di-ethylacetal	112—113	1.3888	1 : 1 : 1.2 : 2	20	24	B	90
4	Butyraldehyde di-ethylacetal	143—145	1.3958	1 : 1 : 0.5 : 2 *	20	48	B	92
5	Isobutyraldehyde di-methylacetal	100—103	1.3875	1 : 1 : 0.5 : 2	60—80	8	A	77
6	Isobutyraldehyde di-ethylacetal	134—136	1.3930	1 : 1 : 0.5 : 2 **	60—80	8	B	97
7	Acetone dimethyl-ketal	78—80	1.3778	1 : 0.9 : 0.5 : 5	60—80	8	A	81
8	Acetone diethylketal	112—114	1.3893	1 : 0.9 : 0.5 : 6	70—90	8	A	93
9	Methyl ethyl ketone dimethylketal	106—107	1.3928	1 : 1 : 0.5 : 6	90—100	8	A	68
10	Methyl ethyl ketone diethylketal	134—135	1.3990	1 : 1 : 0.5 : 6	90—100	8	A	60
11	Cyclohexanone di-methylketal	158—162	1.4367	1 : 1 : 2 : 2	100	8	B	90
12	Cyclohexanone di-ethylketal	75 (15)	1.4370	1 : 1 : 2 : 2	100	8	B	94
13	Cyclopentanone di-ethylketal	77—78 (35)	1.4250	1 : 1 : 1 : 2.5	100	8	B	72
14	Furfural dimethyl-acetal	55—56 (11)	1.4502	1 : 1 : 0.5 : 2	80—90	6	B	98
15	Furfural diethylacetal	76—77 (13)	1.4398	1 : 1 : 0.5 : 2 **	90—100	6	B	97
16	Sorbaldehyde di-ethylacetal	84—85 (12)	1.4535	1 : 1.4 : 0.5 : 5	20	120	B	75
17	Crotonaldehyde di-ethylacetal	147—150	1.4135	1 : 1 : 0.5 : 1.5	20	144	B	56
18	β -Methylcroton-aldehyde diethylacetal	70—72 (25)	1.4204	1 : 1.1 : 0.5 : 2	20	72	B	72

*200 ml ether added to the reaction mixture.

**150 ml benzene added to the reaction mixture.

TABLE 2

Serial No.	Name	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR found	MR calculated	Found C	Found H	Calculated C	Calculated H	Reaction conditions carbonyl compound: tetra-alkoxysilane: alcohol (in moles):85%H_3PO_4 (in ml)	temperature	duration (hr)	method	Yield (%)
19	Crotonaldehyde di-methylacetal	118—120°	1.4096	0.8787	32.79	32.71	62.45, 62.48	10.61, 10.50	62.04	10.41	1 : 1.1 : 0.1 : 1	20°	72	A	82
20	β-Methylcrotonal-dehyde dimethyl-acetal	136—138	1.4207	0.8827	37.17	37.36	64.65, 64.47	10.91, 10.73	64.59	10.83	1 : 1.1 : 0.5 : 2	20	72	B	70
21	Citral diethylacetal	105—106 (10)	1.4548	0.8984	59.85	60.12	72.88, 72.78	11.01, 10.89	72.69	11.19	1 : 1.1 : 0.5 : 1.5	20	48	B	81
22	Citral diethylacetal	117—118 (10)	1.4503	0.8730	69.89	69.42	74.76, 74.60	11.69, 11.67	74.27	11.58	1 : 1.1 : 0.5 : 2	20	48	B	87
23	2-Methylhepten-2-one-6-dimethyl-ketal	74—76 (9)	1.4345	0.8884	50.54	51.19	69.51, 69.51	11.28, 11.48	69.76	11.62	1 : 1.2 : 3 : 10	100	5	B	66
24	2-Methylhepten-2-one-6 diethylketal	83—85 (8)	1.4332	0.8638	60.43	60.30	71.92, 71.69	11.98, 12.01	71.95	12.07	1 : 1.1 : 2.5 : 10	100	10	B	60

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A gelatinous mass is formed some time after the start of the reaction during preparation of the diethyl-acetals of butyraldehyde, isobutyraldehyde and crotonaldehyde. This behavior greatly slows down the reaction, and the yield of acetals is reduced. Gelatinization can be avoided by performing the reaction in inert solvents (benzene or ether).

Two methods of working-up were used for isolation of acetals and ketals from the reaction mass (methods A and B).

When the boiling points of the resulting acetals or ketals are lower than the original tetraalkoxysilanes, it is expedient to distil them from the reaction mass at atmospheric pressure or in low vacuum. Silicon compounds present as impurities are eliminated by treatment of the product with 30% alkali,followed by 2 to 3 washings with water (the latter for removal of alcohol); the products is then dried and distilled (method A) [3]. High-boiling acetals and ketals are isolated from the reaction mass, without prior distillation, by shaking for 0.5 hr with 30% alkali, removal of the alcoholic layer, drying and distillation (method B).

Diethylacetals of crotonaldehyde and methylheptenone were also obtained in good yield with the help of orthoformic ester. In addition, we prepared the cyclic ketal of methylheptenone (methylheptenone ethylene-ketal). Reaction was effected by heating methylheptenone with ethylene glycol in a medium of anhydrous benzene in presence of p-toluenesulfonic acid, and the water of reaction was distilled off simultaneously.

All of the acetals and ketals prepared in this work are set forth in Tables 1 and 2.

EXPERIMENTAL

Dimethylacetal of crotonaldehyde. A mixture of 183 g crotonaldehyde, 436 g tetramethoxysilane, 10.5 ml methyl alcohol and 2.5 ml of 85% phosphoric acid was left for 3 days at room temperature. The odor of crotonaldehyde disappeared completely. The acetal was distilled off in a vacuum (70-75° at 170 mm),treated with 200 ml 30% sodium hydroxide, twice washed with water (up to 200 ml), dried with anhydrous potassium carbonate, and distilled at atmospheric pressure to give 232 g dimethylacetal of crotonaldehyde. The wash waters were extracted with ether, and the ethereal extract was washed with water,dried and distilled. A further 18 g acetal was obtained. Total yield 250 g (82%) of the dimethylacetal of crotonaldehyde (Table 2,No. 19).

Citral diethylacetal. A mixture of 45.6 g citral, 68.6 g tetraethoxysilane, 8.8 ml anhydrous ethyl alcohol and 0.5 ml 85% phosphoric acid was left at room temperature for 2 days and then heated with 150 ml 30% sodium hydroxide. The product was extracted with ether, dried with anhydrous potassium carbonate and distilled in vacuum. Yield 59 g (87%) of citral diethylacetal (Table 2, No. 22).

Crotonaldehyde diethylacetal. A mixture of 82.5 g crotonaldehyde, 150 g orthoformic ester, 40 ml an-hydrous alcohol and 2.8 ml 85% phosphoric acid was left at room temperature for 40 hr. The product was neutralized with ammonia, diluted with an equal volume of ether, washed with water, dried with potassium carbonate and distilled. Yield 113 g (77%) of crotonaldehyde diethylacetal (Table 1, No. 17).

2-Methylhepten-2-one-6 diethylketal. A mixture of 63 g methylheptenone, 74 g orthoformic ester, 70 ml anhydrous ethyl alcohol and 3 drops of concentrated sulfuric acid was left overnight and then heated at 60° for 4.5 hr. The product was poured into 200 ml aqueous ammonia and extracted with 250 ml ether. The ethereal extract was twice washed with water, dried with anhydrous potassium carbonate and distilled in vacuum to give 77.8 g (78%) of methylheptenone diethylketal (Table 2, No. 24).

Methylheptenone ethyleneketal. 42 g methylheptenone, 80 ml anhydrous benzene, 25 g ethylene glycol and 0.3 g p-toluenesulfonic acid were charged into a round-bottomed flask, fitted with water lead-off and reflux condenser. The mixture was boiled for 2 hr, during which period 7 ml water was separated. The product was neutralized with sodium methoxide, extracted with ether, washed with water, and dried with calcium chloride. Distillation gave 37 g (65%) of ketal.

B.p. 51-53° (2 mm), n_D^{20} 1.4503, d_{20}^{20} 0.9313, MR 49.22; calc. 49.00.

Found % C 70.46, 70.68; H 10.68; H 10.28. $C_{10}H_{18}O_2$ Calculated % C 70.50; H 10.58.

SUMMARY

Tetraalkoxysilanes were used in a newly developed method of preparation of acetals and ketals of various aliphatic aldehydes and ketones, α,β-unsaturated aldehydes, and cyclic ketones.

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SYNTHESIS OF VINYL AND DIENIC ETHERS

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Vinyl ethers are each year increasing in importance in organic chemistry thanks to their great reactivity in various chemical transformations. Several methods are known for the preparation of vinyl ethers, of which the following are the most convenient in practice:

1) Reaction of acetylene and its homologs with alcohols in presence of alkali [1,2] (method of A. E. Favorskii and M. F. Shostakovskii).

2) Reaction of vinyl halides with alkoxides or with alcoholic solutions of caustic alkali [3] (method of A. M. Butlerov).

3) Catalytic cleavage of alcohol from acetals [4].

The first two methods have become important mainly for the synthesis of vinyl ethers without substituents in the vinyl group. Vinyl ethers with various substituents in the vinyl group are more conveniently prepared by catalytic decomposition of acetals and ketals (method 3).

Not long ago we published our method of synthesis of various acetals and ketals with the help of tetra-alkoxysilanes [6].

We have also utilized the prepared acetals and ketals for the synthesis of vinyl ethers containing various substituents in the vinyl group.

Sigmund and Uchan [4] established the possibility of splitting off an alcohol and forming vinyl ethers by passing the vapors of acetals over granules of clay. But the yields were very low, due to formation of secondary products such as acetaldehyde and crotonaldehyde, carbon monoxide and methane. This method was later improved by Reppe [5] by using noble metals as catalysts (silver, gold and platinum).

We made use of phosphates — NaH_2PO_4 and $MgHPO_4$ — as catalysts for detachment of alcohol from acetals. Passage of vapors of the dimethyl and diethylacetals of acetaldehyde, propionaldehyde, butyraldehyde and isobutyraldehyde, also of the dimethyl- and diethylacetals of acetone and cyclohexanone, over these catalysts at 300-375° led to the corresponding substituted vinyl ethers (Table 1).

It was shown by Meier [7], and a little later by Flaig [8] and Faimilo [9], that acetals of crotonaldehyde and β-alkoxyacetals of butyraldehyde (1,1,3-trialkoxybutanes) are converted into dienic ethers (1-alkoxy-1,3-butadienes) on passage over certain catalysts at 250-350°.

Wichterle [10] reported the preparation of 1-alkoxy-1,3-butadienes by prolonged treatment of acetals of β-chlorobutyraldehyde with potassium hydroxide. Flaig [8], however, failed to obtain 1-alkoxybutadienes by this route.

Dienic ethers are of great interest in organic chemistry. The two conjugated double bonds and the reactivity of the alkoxyl group are indicative of great synthetic possibilities.

Special interest is attached to the alkoxyisoprenes (1-alkoxy-3-methyl-1,3-butadienes) whose methyl group in the 3 position endows them with an isoprenoid structure that permits them to be used for the synthesis of important isoprenoids [11, 12] (dehydrocitral, farnesinal, vitamin A, carotene, etc.).

In the present work we realized for the first time, and developed, the synthesis of methoxy- and ethoxyiso-prenes, and we also studied the synthesis of methoxy- and ethoxybutadienes described previously [7, 8, 9].

The alkoxydienes in question were prepared by catalytic decomposition of acetals of crotonaldehyde and β -methylcrotonaldehydes, as well as of 1,1,3-trialkoxybutanes and 1,1,3-trialkoxy-3-methylbutanes.

Dimethyl- and diethylacetals of β -methylcrotonaldehyde were prepared by the following reactions [13]:
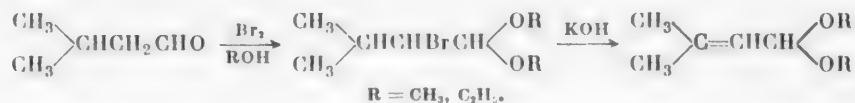
$$\underset{CH_3}{\overset{CH_3}{>}}CHCH_2CHO \xrightarrow[ROH]{Br_2} \underset{CH_3}{\overset{CH_3}{>}}CHCHBrCH\underset{OR}{\overset{OR}{<}} \xrightarrow{KOH} \underset{CH_3}{\overset{CH_3}{>}}C=CHCH\underset{OR}{\overset{OR}{<}}$$

$$R = CH_3, C_2H_5.$$

TABLE 1

Serial No.	Acetal or ketal	Reaction temperature	Rate of passage (g/hr)	Vinyl ether*	Boiling point	n_D^{20}	Yield** (in %)
1	$CH_3CH(OCH_3)_2$	375°	41	$CH_2=CHOCH_3$	7—8°	—	67
2	$CH_3CH(OC_2H_5)_2$	325	67	$CH_2=CHOC_2H_5$	34—36	1.3780	73
3	$CH_3CH_2CH(OCH_3)_2$	325	84	$CH_3CH=CHOCH_3$	45—47	1.3758	74
4	$CH_3CH_2CH(OC_2H_5)_2$	320	75	$CH_3CH=CHOC_2H_5$	69	1.3988	75
5	$CH_3CH_2CH_2CH(OCH_3)_2$	325	53	$CH_3CH_2CH=CHOCH_3$	74—77	1.3995	70
6	$CH_3CH_2CH_2CH(OC_2H_5)_2$	325	60	$CH_3CH_2CH=CHOC_2H_5$	94	1.4050	75
7	$(CH_3)_2CHCH(OCH_3)_2$	325	60	$(CH_3)_2C=CHOCH_3$	70—73	1.3965	60
8	$(CH_3)_2CHCH(OC_2H_5)_2$	325	60	$(CH_3)_2C=CHOC_2H_5$	88—90	1.4046	75
9	$(CH_3)_2C(OCH_3)_2$	325	60	$CH_2=C(CH_3)OCH_3$	38—39	1.3738	77
10	$(CH_3)_2C(OC_2H_5)_2$	300	100	$CH_2=C(CH_3)OC_2H_5$	60—63	1.3929	68
11	(ring, OCH_3, OCH_3)	340	75	(ring, $-OCH_3$)	140—143	1.4590	73
12	(ring, OC_2H_5, OC_2H_5)	325	50	(ring, $-OC_2H_5$)	156—158	1.4560	76

*Vinyl methyl ether was prepared with use of NaH_2PO_4 as catalyst; all the remaining ethers in the table with use of $MgHPO_4 \cdot Na_2SiO_3$.

**Yields are calculated on acetal or ketal passed through.

1,1,3-Trimethoxybutane and 1,1,3-triethoxybutane were prepared by addition to crotonaldehyde of the appropriate alcohols in presence of hydrogen chloride [7].

In addition, we prepared 1,1,3-triethoxybutane from vinyl ethyl ether and alcohol according to the scheme:

$$C_2H_5OH \xrightarrow[HCl]{CH_2=CHOC_2H_5} CH_3CH\underset{OC_2H_5}{\overset{OC_2H_5}{<}} \xrightarrow[BF_3 \cdot O(C_2H_5)_2]{CH_2=CHOC_2H_5} \underset{CH_3CHCH_2CH}{\overset{OC_2H_5}{|}}\underset{OC_2H_5}{\overset{OC_2H_5}{<}}$$
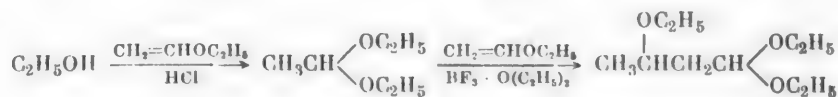
The whole of this process can be realized in a single operation without isolation of acetaldehyde diethyl-acetal in the pure state. Condensation of the first molecule of vinyl ethyl ether with alcohol in presence of traces of hydrochloric acid gives the acetal [14]; to this is added a little boron fluoride trietherate as catalyst, and a second molecule of vinyl ethyl ether is added on [15].
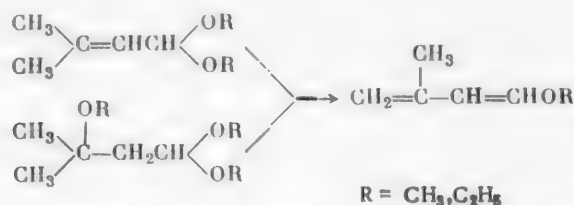
We synthesized 1,1,3-trialkoxy-3-methylbutanes, needed for preparation of alkoxyisoprenes, in analogous fashion by condensing acetone ketals with vinyl alkyl ethers [11].

In order to avoid further condensation of the resulting 1,1,3-trialkoxy-3-methylbutane with the vinyl ether, it is necessary to bring a 50% excess of acetone ketal into reaction.

Hardly anything is known about the addition of ketals to vinyl ethers. The only published information is in a patent on the addition of ketals of acetone and cyclohexanone to vinyl methyl ether in low yield [16].

Catalytic breakdown of acetals of crotonaldehyde, β-methylcrotonaldehyde and trialkoxybutanes to dienic ethers was effected over NaH_2PO_4 and $MgHPO_4$. Active carbon, silica gel and glass wool were used as carriers for these catalysts.

The reaction was conducted in vacuum (10-20 mm) in a nitrogen stream.

$$\begin{array}{c} CH_3 \\ \diagdown \\ C=CHCH\diagup^{OR}_{OR} \\ CH_3 \diagup \end{array}$$

$$\begin{array}{c} OR \\ CH_3 \diagdown \diagup \\ C-CH_2CH\diagup^{OR}_{OR} \\ CH_3 \diagup \end{array} \longrightarrow \begin{array}{c} CH_3 \\ | \\ CH_2=C-CH=CHOR \end{array}$$

$$R = CH_3, C_2H_5$$

Catalytic breakdown of 1,1,3-triethoxy-3-methylbutane to ethoxyisoprene was studied over the following catalysts: $MgHPO_4 \cdot Na_2SiO_3$, $MgHPO_4$ on active carbon, NaH_2PO_4, and $NaH_2PO_4(\cdot)$(the last two on silica gel). The maximum yield of ethoxyisoprene is obtained with $MgHPO_4$ on active carbon and with $MgHPO_4 \cdot Na_2SiO_3$ (Table 2).

The active life of these catalysts was also investigated. $MgHPO_4$ on carbon was the most stable catalyst; after 10-hour's working.the yield of ethoxyisoprene fell from 74 to 59%. The activity of catalysts prepared from NaH_2PO_4 falls off very much faster. After only 5 hours the yield of ethoxyisoprene over these catalysts fell to 38%.

We also investigated the catalytic breakdown of 3-methyl-1,3-dimethoxy-1-ethoxybutane and found that the reaction gives a mixture of methoxy- and ethoxyisoprenes in approximately equal quantities.

EXPERIMENTAL

1,1,3-Triethoxybutane. 3-4 drops of concentrated hydrochloric acid was added with vigorous stirring to a mixture of 264 g vinyl ethyl ether and 215 ml ethyl alcohol cooled to -12°. The temperature slowly rose to 0° and then rapidly to 55°. The mixture was stirred for a further 0.5 hr; 0.5 ml boron fluoride etherate was then added; this was followed by addition of 80 g vinyl ethyl ether at 40° in the course of 40 minutes from a dropping funnel. The mixture was stirred 1.5 hr at 55°, neutralized with sodium ethoxide and distilled. 291 g of acetaldehyde acetal was obtained with b.p. 102-104° and 128.5 g 1,1,3-triethoxybutane with b.p. 76-78° (10 mm).

α-Bromoisovaleraldehyde dimethylacetal. Into a 3-necked flask, fitted with reflux condenser, mechanical stirrer and dropping funnel, were charged 345 g isovaleraldehyde and 450 ml dry chloroform. 205 ml bromine in 200 ml dry chloroform was introduced into the mixture (cooled to -25 to -30°) in the course of 5 hr in presence of the light from a quartz lamp. In the course of 2 hr the temperature of the mixture rose to +5°; at this stage 1650 ml anhydrous methanol was added and the reaction mass was stood at room temperature for 2 days. The product was poured into a solution of 160 g sodium hydroxide and 40 g sodium carbonate in 5 liters water. The lower chloroform layer was separated and the upper layer extracted with chloroform. The chloroform extracts were combined, dried with calcium chloride and distilled to give 541 g (66%) of α-bromoisovaleraldehyde dimethylacetal with b.p. 71-74° (16 mm), n_D^{20} 1.4587.

The diethylacetal of α-bromoisovaleraldehyde was similarly prepared; yield 72%; b.p. 82-85%, n_D^{20} 1.4462 [13].

TABLE 2

Prep. No.	Acetal* or ketal	Catalyst (in g)	Temperature	Rate of passage (g/hr)	Alkoxydiene: boiling point (pressure in mm) n_D^{20}, d_4^{20}, MR found, MR calculated	Yield** (in %)
1	$CH_3CH=CHCH \big\langle {OCH_3 \atop OCH_3}$	$MgHPO_4 \cdot Na_2SiO_3$ (48)	350°	25		67
2	$CH_3CHCH_2CH \big\langle {OCH_3 \atop OCH_3}$ (OCH$_3$)	NaH_2PO_4 (66)	320	28	$CH_2=CH-CH=CHOCH_3$ 90—91°, 1.4615, 0.8315, 27.78; 26.13	61
		$MgHPO_4 \cdot Na_2SiO_3$ (48)	350	20		64
3	$CH_3CH=CHCH \big\langle {OC_2H_5 \atop OC_2H_5}$		350	60		79
4	$CH_3CHCH_2CH \big\langle {OC_2H_5 \atop OC_2H_5}$ (OC$_2$H$_5$)	NaH_2PO_4 (60)	320	40	$CH_2=CH-CH=CHOC_2H_5$ 65—67 (150), 1.4615	72
5	$CH_3 \atop CH_3 \rangle C=CHCH \big\langle {OCH_3 \atop OCH_3}$		350	29	$CH_3 \atop CH_3 \rangle C=CH-CH=CHOCH_3$	71
6	$CH_3 \atop CH_3 \rangle C-CH_2CH \big\langle {OCH_3 \atop OCH_3}$ (OCH$_3$)	$MgHPO_4 \cdot Na_2SiO_3$ (48)	350	27	115—116, 1.4653, 0.8403, 32.31; 30.77	71
7	$CH_3 \atop CH_3 \rangle C=CHCH \big\langle {OC_2H_5 \atop OC_2H_5}$	NaH_2PO_4 (60)	320	36		55
8	$CH_3 \atop CH_3 \rangle C-CH_2CH \big\langle {OC_2H_5 \atop OC_2H_5}$ (OC$_2$H$_5$)	NaH_2PO_4, $NaH_2PO_4 \cdot SiO_2$ (65)	305	40	$CH_3 \atop CH_3 \rangle C=CH-CH=CHOC_2H_5$ 75—77 (90), 1.4618, 0.8345, 36.87; 35.23	64
			350	55		74
		$MgHPO_4$ on carbon	300	55		74
		$MgHPO_4 \cdot Na_2SiO_3$ (55)	350—390	75		77

• Reaction in vacuum (10-20 mm).

•• Yields based on acetal or alkoxyacetal passed over.

β-Methylcrotonaldehyde dimethylacetal. A mixture of 100 g potassium hydroxide and 328 g α-bromo-isovaleraldehyde dimethylacetal was heated with vigorous stirring at 140-145° in a nitrogen atmosphere for 6 hours. The reaction product was distilled in vacuum (about 30 mm), 200 g potassium hydroxide was added to it, and the mixture was heated for a further 6 hr at 140-150°. The resulting acetal was distilled in vacuum.(b.p. 62-65° at 55 mm) and dried with anhydrous potassium carbonate. Redistillation gave 144 g (71%) of β-methyl-crotonaldehyde dimethylacetal with b.p. 135-138°, n_D^{20} 1.4200.

β-Methylcrotonaldehyde diethylacetal was similarly prepared in 88% yield; b.p. 60-62° (17 mm), n_D^{20} 1.4190 [13].

1,1,3-Triethoxy-3-methylbutane. 1300 g acetone diethylketal and 5.2 ml boron fluoride etherate were charged into a three-necked flask, equipped with mechanical stirrer, dropping funnel, reflux water condenser, dropping funnel and thermometer. The mixture was cooled with iced water to 3-4°, and at this temperature 500 g vinyl ethyl ether was stirred in over a period of 3.5 hr. Stirring was continued for a further 3.5 hr, after which the mixture was neutralized with sodium ethoxide and distilled. 695 g substance with b.p. 90-120° was obtained. It was washed twice with water, dried with potassium carbonate, and redistilled to give 615 g of un-changed acetone diethylketal (b.p. 110-114°) and 903 g 1,1,3-triethoxy-3-methylbutane.

B.p. 83-85° (11 mm), n_D^{20} 1.4145, d_{20}^{20} 0.8813 MR 58.01; calc. 57.92.

Found % C 64.55, 64.45; H 11.80, 11.77. $C_{11}H_{24}O_3$. Calculated % C 64.66; H 11.84.

The yield was 64% calculated on the vinyl ether, and 85% calculated on the reacted ketal. Residue in flask 207 g.

1,1,3-Trimethoxy-3-methylbutane. To a mixture of 170 g acetone dimethylketal and 0.8 ml boron fluoride etherate at 0-2° was added 70 g vinyl methyl ether (with stirring) in the course of 2 hr from a dropping funnel cooled with dry ice. The temperature then rose to room temperature in the course of 1.5 hr, and the reaction mixture was neutralized with sodium methoxide and distilled. There was obtained 100 g of unchanged acetone dimethylketal with b.p. 75-85° and 95 g 1,1,3-trimethoxy-3-methylbutane.

B.p. 75-77° (25 mm), n_D^{20} 1.4117, d_{20}^{20} 0.9274, MR 43.49; calc. 44.07.

Found % C 59.41, 59.20; H 11.23, 11.15. $C_8H_{18}O_3$. Calculated %: C 59.23; H 11.18.

Yield calculated on the vinyl ether 48%, on the reacted ketal 90%.

1,3-Dimethoxy-1-ethoxy-3-methylbutane. 76.8 g vinyl ethyl ether was added to a mixture (cooled to 4°) of 251.5 g acetone dimethylketal and 0.8 ml boron fluoride etherate in the course of 1.5 hr. The reaction mass was cooled for a further 0.5 hr and held for 1 hr at room temperature; it was then neutralized with sodium methoxide and distilled to give 202 g unchanged acetone dimethylketal (b.p. 75-85°) and 87 g 1,3-dimethoxy-1-ethoxy-3-methylbutane.

B.p. 71-73° (14 mm), n_D^{20} 1.4131, d_{20}^{20} 0.9124, MR 48.20; calc. 48.68.

Found %: C 61.46, 61.16; H 11.30; 11.40. $C_9H_{20}O_3$. Calculated % C 61.33; H 11.44.

Yield calculated on the vinyl ether 46%, on the reacted ketal 85%

NaH$_2$PO$_4$ catalyst. Monosodium phosphate (2 moles of water) was placed in a porcelain dish and fused over a bare flame. The water of crystallization came off when the mass was stirred with a spatula, and a viscous paste was formed. The hot mass was pressed through a 2.5-mm-mesh screen to give rods 3-4 mm long. The catalyst was freed from residual water by calcination for 2-3 hr at 350° in a 10-15 mm vacuum.

NaH$_2$PO$_4$-on-SiO$_2$ catalyst. 37 g silica gel was heated to incandescence in a muffle furnace and quickly poured with intensive stirring into 27 ml of 1.26 M NaH$_2$PO$_4$ solution. The resulting catalyst was dried at 350°.

MgHPO$_4$·Na$_2$SiO$_3$ catalyst. 160 g dimagnesium phosphate (heptahydrate) was mixed in a mortar with 216 ml water glass (d 1.384). After 2 to 3 hr the mixture set and was extruded through a 2.5-mm-mesh screen. The extruded shapes were cut to a length of 3-4 mm and dried for 2 hr in a drying cupboard at 100° before being calcined 2 hr at 350°.

MgHPO$_4$-on-carbon catalyst. 75 ml active carbon (AR grade) was poured into a mixture of 15 g MgHPO$_4$ in 100 ml boiling water, and the mixture was boiled 4 hr. The catalyst was filtered off, dried at 150° and sifted from the residue of MgHPO$_4$.

Design of a catalytic apparatus for preparation of vinyl ethers and alkoxydienes. Catalytic decomposition of acetals and alkoxyacetals was carried out in a furnace 60 cm long containing a tube 20 mm in diameter. The acetal or alkoxyacetal was introduced dropwise, from a Balandin buret, into a vaporizer in which a temperature of 150-180° was maintained and from which the vapor passed into the catalytic tube. The outlet of the latter was joined to a receiver which could be cooled if necessary with dry ice and acetone. The receiver had to contain a small quantity of anhydrous potassium carbonate for neutralization of traces of acid catalyst entrained with the vapor of the compound. In this way the reverse reaction of addition of alcohols to vinyl ethers was prevented.

When the reaction was run in vacuo, the apparatus was equipped with two vacuum gauges for measurement of the vacuum in the vaporizer and the receiver. The vaporizer was provided with a capillary through which dry nitrogen was admitted. A 15-40-mm vacuum was created in the system by means of a water-jet pump.

Propenyl ethyl ether (1-ethoxy-1-propene). 150 g propionaldehyde diethylacetal was passed through the catalytic tube, containing 40 g MgHPO$_4$·Na$_2$SiO$_3$ catalyst, at 320° for 2.5 hr. The condensate was washed with 5% potassium carbonate solution, dried with anhydrous potassium carbonate and distilled. Yield 98 g (75%) of propenyl ethyl ether with b.p. 69°, n_D^{20} 1.3988.

The other vinyl ethers listed in Table 1 were similarly prepared.

1-Methoxy-3-methyl-1,3-butadiene (methoxyisoprene). 29 g β -methylcrotonaldehyde dimethylacetal was passed through the reaction tube, which contained 48 g of MgHPO$_4$ Na$_2$SiO$_3$ catalyst, at 350° for 1 hr in a 40-mm vacuum. The receiver was cooled with dry ice and acetone. The substance was washed with 5% sodium bicarbonate solution and twice with water, dried with anhydrous potassium carbonate and distilled. Yield 15.5 g (71%) of 1-methoxy-3-methyl-1,3-butadiene with b.p. 115-116°.

Found %: C 73.35, 73.45; H 10.23, 10.34. C$_6$H$_{10}$O. Calculated %: C 73.41; H 10.27.

In this experiment 2.5 g of unchanged acetal was recovered; b.p. 135-138°.

1-Ethoxy-3-methyl-1,3-butadiene (ethoxyisoprene). 600 g 1,1,3-triethoxy-3-methylbutane was passed through the reaction tube, which contained 55 g of MgHPO$_4$ · Na$_2$SiO$_3$ catalyst, for 8 hr in a 15-mm vacuum at 350-390° (the last 150 g at 390°). The receiver was cooled with dry ice and acetone. The condensate was washed 3 times with 5% potassium carbonate solution and dried with anhydrous potassium carbonate. Distillation gave 254 g 1-ethoxy-3-methyl-1,3-butadiene with b.p. 75-77° (90 mm).

Found %: C 75.23, 75.25; H 10.85, 10.71. C$_7$H$_{12}$O. Calculated %: C 75.00; H 10.71.

51 g of 1,1,3-triethoxy-3-methoxybutane was recovered unchanged; b.p. 80-85° (10 mm).

The yield of ethoxyisoprene was 77% calculated on the ethoxyacetal introduced and 85% on the alkoxy-acetal reacted.

SUMMARY

1. A study was made of the synthesis of vinyl ethers by catalytic decomposition of acetals and ketals over phosphates (MgHPO$_4$ and NaH$_2$PO$_4$).

2. The condensation of acetone ketals with vinyl ethers in presence of boron trifluoride etherate was studied. 1,1,3-Trialkoxy-3-methylbutanes were obtained in good yield.

3. Vinyl ethers were synthesized from acetals of crotonaldehyde, β -methyl-crotonaldehyde and 1,1,3-trialkoxybutanes.

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THE CYANOETHYLATION OF 3-QUINUCLIDONE

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The reaction of acrylonitrile with ketones of the aliphatic, cyclic and fatty-aromatic series has been studied fairly extensively. The study of the cyanoethylation reaction is especially interesting because of the great synthetic possibilities afforded by the introduction of the cyanoethyl group into the molecules of ketones. Very little work has been done, however, on the cyanoethylation of heterocyclic ketones. Attention may be drawn to the cyanoethylation of alkyl-substituted 4-piperidones and γ-pyrones, which has been fully described by I. N. Nazarov and co-workers [1].

The cyanoethylation of 3-quinuclidone has not previously been studied and is a subject of considerable interest. It is studied in the present work.

A mixture of mono- and dicyanoethylated substances is formed when 3-quinuclidone is reacted with a large excess of acrylonitrile in dioxane or tert-butyl alcohol in presence of a 30% solution of potassium hydroxide in methyl alcohol. The total yield of cyanoethylation products and the "mono/di ratio" depend on the solvent used. About 44% of cyanoethylated derivatives is formed in dioxane. In this case the main component of the mixture (85%) is dicyanoethylated 3-quinuclidone. Replacement of dioxane by tert-butyl alcohol leads to an increase of the over-all yield to 70% and the proportion of monocyanoethylated 3-quinuclidone rises to about 35% of the total yield. It should be noted that the yield of cyanoethylated products does not exceed 10% if 3-quinuclidone is brought into reaction with only the equimolar quantity of acrylonitrile.

For the purpose of establishment of the position of the cyanoethyl group in monocyanoethylated 3-quinuclidone, the product was heated with a mixture of acetic and hydrochloric acids and thereby converted into the corresponding β-substituted propionic acid; the latter in turn was esterified to the ester of propionic acid by treatment with an alcoholic solution of hydrogen chloride. The resulting ketoester was reduced with hydrazine hydrate in presence of an alcoholic solution of sodium ethoxide to give a compound which was identical with the previously synthesized [2] 2-(β-carboxyethyl)-quinuclidine.

Monocyanoethylated 3-quinuclidone consequently has the structure of 3-keto-2-(β-cyanoethyl)-quinuclidine (II).

Reduction of 3-keto-2-(β-carbethoxyethyl)quinuclidine (IV) with lithium aluminum hydride gave 3-hydroxy-2-(γ-hydroxypropyl)-quinuclidine (VI).

The steps in the synthesis may be represented by the scheme on the following page.

(A)
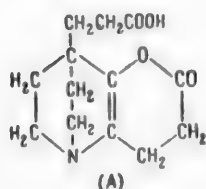
Dicyanoethylated 3-quinuclidone may have the structure of 2,2- or 2,4-di-(β-cyanoethyl)-3-quinuclidone. Saponification of the ketodinitrile gives a ketodiacid which on heating with acetic anhydride is not converted into the tricyclic unsaturated compound (A) as would have happened if the cyanoethyl groups had been in the 2 or 4 position. Transformations of a similar type have been described for 1-(β-carboxyethyl)-2-cyclohexanone; heating with acetic anhydride converts this compound into $\Delta^{9, 10}$-hexahydrocoumarin [3].

In the light of the foregoing facts we suggest that dicyanoethylated 3-quinuclidone is 3-keto-2,2-di-(β -cyanoethyl)-quinuclidine (VII). The product of its hydrolysis with a mixture of acetic and hydrochloric acids was 3-keto-2,2-di-(β -carboxyethyl)-quinuclidine (VIII);the latter was esterified to 3-keto-2,2-di-(β -carbethoxyethyl)-quinuclidine (IX), reduction of which with lithium aluminum hydride gave 3-hydroxy-2,2-di-(γ -hydroxypropyl)-quinucline (X), while treatment with hydrazine hydrate gave the corresponding dihydrazide(XI).

Reaction of ester (IX) with hydrazine hydrate in presence of sodium ethoxide at 180° led to 2,2-di-(β-carbethoxyethyl)-quinuclidine (XII), which on treatment with hydrochloric acid was transformed into the hydrochloride of 2,2-di-(β-carboxyethyl)-quinuclidine (XIII). Reduction of 3-keto-2,2-di-(β-cyanoethyl)-quinuclidine (VII) with lithium aluminum hydride gave 3-hydroxy-2,2-di-(β-cyanoethyl)-quinuclidine (XIV).

EXPERIMENTAL

3-Quinuclidone (I). 24 g of metallic potassium was put into 100 ml anhydrous toluene and 36 ml anhydrous alcohol was stirred in. The reaction mass was heated to 120-125° (bath temperature) and in the course of an hour a solution of 60 g 1-carbethoxymethyl-4-carbethoxypiperidine in 150 ml toluene was added at the same temperature. After the diester had been added, the mixture was stirred at the boiling point of toluene for 5 hr. Addition was thereupon made of 200 ml concentrated hydrochloric acid and the mixture was stirred 30 minutes. The hydrochloric acid layer was then separated from the toluene layer in a separating funnel. The toluene layer was twice-extracted with concentrated hydrochloric acid (200 ml each time), and the hydrochloric acid solutions were combined and boiled 15 hr. The solution was decolorized with carbon and evaporated on a steam bath. To the residue (cooled) was added 70 ml 50% potassium hydroxide; the alkaline solution extracted with benzene, the benzene solution was dried with potassium carbonate, and the benzene was taken off in vacuo to leave 25.6 g (84.6%) of 3-quinuclidone. M. p. 136-138°; picrate m.p. 210° [4].

Cyanoethylation of 3-quinuclidone. A. To a solution of 25 g 3-quinuclidone in 115 ml anhydrous dioxane was added 3.8 ml of 30% solution of potassium hydroxide in methyl alcohol, and the reaction temperature was raised to 60°. At this temperature 90 ml acrylonitrile was stirred in over a period of 30 minutes, after which the reaction mass was stirred at the same temperature for a further 4 hr. The resulting polyacrylonitrile (a yellowish-brown amorphous precipitate) was filtered off and the dioxane was taken off in vacuo. To the residue was added 100 ml benzene, and the benzene solution was extracted with 50 ml 10% hydrochloric acid. The hydrochloric acid solution was treated with calcined potassium carbonate to saturation point, and then exhaustively extracted with benzene. The benzene solution was dried with potassium carbonate and the benzene was distilled off. The residue was sublimed (at 20 mm, bath temperature 125-130°) to give 14.3 g 3-quinuclidone and the residual viscous, brown mass was diluted with a mixture of 20 ml anhydrous alcohol and 1 ml anhydrous benzene. The resulting precipitate of 3-keto-2,2-di-(β-cyanoethyl)-quinuclidine was filtered and thoroughly washed with alcohol. There was obtained 4 g of colorless crystals, readily soluble in chloroform, benzene and hot alcohol; insoluble in ether and water. M.p. 120-122° (from alcohol).

Found %: C 68.00; H 7.47; N 18.24. $C_{13}H_{17}ON_3$. Calculated %: C 67.75; H 7.36; N 18.18.

After separation of the 3-keto-2,2-di-(β-cyanoethyl)-quinuclidine, the mother liquor was twice-distilled in vacuo to give 0.7 g 3-keto-2-(β-cyanoethyl)-quinuclidine with b.p. 121-122° (0.3 mm). The compound is a colorless, mobile liquid, readily soluble in organic solvents, insoluble in water.

Found %: C 67.09; H 7.93; N 15.72, 15.68. $C_{10}H_{14}ON_2$. Calculated %: C 67.41; H 7.86; N 15.73.

B. 60 ml of acrylonitrile was added at 60-65° to a solution of 15 g 3-quinuclidone in 75 ml anhydrous tert-butyl alcohol containing 2.3 ml 30% solution of potassium hydroxide in methyl alcohol. After treatment similar to that in A, 3.6 g 3-quinuclidone was recovered unchanged, and from the reaction products were isolated 6.52 g 3-keto-2,2-di-(β-cyanoethyl)-quinuclidine, 3.48 g 3-keto-2-(β-cyanoethyl)-quinuclidine and 5.38 g of a mixture of these compounds which was directly converted to the corresponding acids. The latter were fractionated on the basis of their differing solubilities in hot alcohol.

3-Keto-2-(β-carbethoxyethyl)-quinuclidine (IV). 3.48 g 3-keto-2-(β-cyanoethyl)-quinuclidine, 60 ml glacial acetic acid and 30 ml concentrated hydrochloric acid were boiled 20 hr. The solution was decolorized with carbon and evaporated on a water bath. The resulting cyrstalline mass, containing the hydrochloride of 3-keto-2-(β-carboxyethyl)-quinuclidine and ammonium chloride, was heated at the boil with 40 ml 9% alcoholic solution of hydrogen chloride for 3 hr. The alcohol was taken off in vacuo and the residue again heated alcoholic hydrogen chloride. After the alcohol had been removed, the reaction mass was treated with 50% potassium carbonate solution and extracted with ether. The ethereal solution was dried with potassium carbonate, the ether was driven off, and the compound was distilled in vacuo. There was obtained 2.6 g (60.6%) of 3-keto-2-(β-carbethoxyethyl)-quinuclidine in the form of a colorless, mobile liquid, soluble in organic solvents and insoluble in water. B.p. 136-138° (0.4 mm).

Found %: C 63.58; H 8.54; N 6.46, 6.10. $C_{12}H_{19}O_3N$. Calculated %: C 64.00; H 8.45; N 6.22.

Hydrochloride of 3-keto-2-(β -carboxyethyl)quinuclidine (III). 1 g 3-keto-2-(β -carbethoxyethyl)-quinuclidine and 10 ml 17% hydrochloric acid were boiled 4 hr. The solution was decolorized with carbon and the hydrochloric acid was taken off in vacuo. The residue was triturated with anhydrous alcohol and the crystals were filtered off. There was obtained 1 g (96.5%) hydrochloride in the form of a white crystalline powder, readily soluble in water and hot alcohol. M.p. 191-193° (with decomp.) (from alcohol).

Found %: C 48.22; H 7.32; N 5.77; Cl 14.09. $C_{10}H_{16}O_3NCl \cdot H_2O$. Calculated %: C 47.72; H 7.16; N 5.57; Cl 14.11.

Hydrochloride of 2-(β -carboxyethyl)-quinuclidine (V). To a solution of sodium ethoxide in ethyl alcohol, prepared from 0.4 g metallic sodium and 9 ml anhydrous alcohol, were added 0.3 g 3-keto-2-(β -carbethoxy-ethyl)-quinuclidine and 1.8 ml hydrazine hydrate. The mixture was heated in a sealed tube at 170-180° for 14 hr. The alcohol was then distilled off in vacuo, the solid residue was dissolved in 10 ml water, and the aqueous solution was boiled 4 hr. The reaction mass was acidified with concentrated hydrochloric acid until it had an acid reaction to Congo, and the solution was then evaporated to dryness on a steam bath. The solid residue contained a considerable amount of inorganic salts in addition to the hydrochloride of 2-(β-carboxyethyl)-quinuclidine. The dry residue was therefore heated with 10 ml 10% alcoholic hydrogen chloride for 3 hr. The alcohol was taken off in vacuo and the residue was treated with 50% potassium carbonate solution and extracted with ether. The ethereal solution was dried with potassium carbonate, the ether was distilled off, and the residue was distilled in vacuo to give 0.17 g 2-(β -carbethoxyethyl)-quinuclidine in the form of a colorless, mobile liquid, readily soluble in organic solvents, poorly soluble in water. B. p. 90-92° (0.2 mm).

The compound was boiled 4 hr with 4 ml 17% hydrochloric acid. The hydrochloric acid solution was decolorized with carbon and evaporated in vacuo, and the residue was crystallized from anhydrous alcohol. 0.06 g hydrochloride of 2-(β -carboxyethyl)-quinuclidine was obtained in the form of a white, crystalline powder, easily soluble in water, poorly soluble in alcohol, insoluble in ether, benzene and acetone. M.p. 216.5-217.5° (decomp.) [2]. No depression of melting point in admixture with the acid prepared from 2-formylquinuclidine.

Found %: C 54.73, 54.60; H 8.28, 8.28; N 6.69, 6.40; Cl 15.94, 16.00. $C_{10}H_{18}O_2NCl$. Calculated %: C 54.67; H 8.20; N 6.38; Cl 16.17.

3-Hydroxy-2-(γ -hydroxypropyl)-quinuclidine (VI). A solution of 0.75 g 3-keto-2-(β -carbethoxypropyl)-quinuclidine in 15 ml anhydrous ether was stirred into a suspension of 0.5 g lithium aluminum hydride in 20 ml anhydrous ether. The mixture was heated 3 hr at the boiling point of ether. Addition was then made (with cooling) of 1.5 ml water, and the inorganic salts were filtered and well washed with chloroform. The ether-chloroform extract was evaporated in vacuo and the residue distilled. B.p. 163-165° (0.4 mm). A colorless liquid, readily soluble in water and organic solvents. Yield 0.35 g (56.7%). The hydrochloride melts at 132-133°. Colorless crystals, readily soluble in water and alcohol, insoluble in ether, acetone, benzene and chloroform.

Found %: C 54.16; H 8.87; N 6.23; Cl 16.04. $C_{10}H_{20}O_2NCl$. Calculated %: C 54.19; H 9.03; N 6.33; Cl 16.03.

Hydrochloride of 3-keto-2,2-di-(β -carboxyethyl)-quinuclidine (VIII). 4.35 g 3-keto-2,2-di-(β -cyanoethyl)-quinuclidine, 80 ml glacial acetic acid and 40 ml concentrated hydrochloric acid were heated at the boil for 17 hr. The acid solution was decolorized with carbon and evaporated to dryness on a steam bath. The solid residue, containing the hydrochloride of 3-keto-2,2-di-(β -carboxyethyl)-quinuclidine and ammonium chloride, was recrystallized from 220 ml 90% alcohol. There was obtained 5.3 g (92% of the hydrochloride of the diacid as colorless crystals, sparingly soluble in alcohol, insoluble in ether, benzene, acetone and chloroform, soluble in water. M.p. 245° (decomp.).

Found %: C 50.65, 50.77; H 6.59, 6.54; N 4.38; Cl 11.61, 11.52. $C_{13}H_{20}O_5NCl$. Calculated %: C 51.06; H 6.55; N 4.58; Cl 11.62.

3-Keto-2,2-di-(β -carbethoxyethyl)-quinuclidine (IX). 6.5 g of the hydrochloride of 3-keto-2,2-di-(β -carboxyethyl)-quinuclidine and 70 ml 9% alcoholic hydrogen chloride were boiled 4 hr. The hydrochloride of the diester came down on cooling and was filtered off, dried in the air, treated with 50% potassium carbonate

until alkaline to phenolphthalein, and extracted with chloroform. The chloroform solution was dried with potassium carbonate, the chloroform was taken off in vacuo, and the residual crystalline mass was distilled to give 4.4 g (63.6%) of diester in the form of colorless crystals, easily soluble in alcohol, ether, chloroform and benzene, soluble in hot ligroin. insoluble in water. B.p. 190° (1 mm), m.p. 58-61°.

Found %: C 63.05, 62.93; H 8.15, 8.20; N 4.19. $C_{17}H_{27}O_5N$. Calculated % C 62.78; H 8.31; N 4.32.

The hydrochloride forms colorless crystals, readily soluble in water, soluble in hot alcohol, insoluble in ether and benzene. M.p. 169-171° (from alcohol).

Found % C 56.15; H 7.70; N 3.80; Cl 9.82. $C_{17}H_{28}O_5NCl$. Calculated % C 56.43; H 7.75; N 3.87; Cl 9.82.

3-Hydroxy-2,2-di-(γ-hydroxypropyl)-quinuclidine (X). To a suspension of 1 g lithium aluminum hydride in 20 ml anhydrous ether was added a solution of 1.57 g 3-keto-2,2-di-(β-carbethoxyethyl)-quinuclidine in 30 ml ether. The reaction mass was heated 3 hr at the boil and treated in the cold with 2 ml water ; the precipitate was filtered and washed with chloroform. The filtrate was evaporated in vacuo. The solid residue was triturated with ether and the precipitate was filtered. Yield 1.17 g (85%) of hygroscopic, colorless crystals, readily soluble in water, alcohol, acetone and chloroform, insoluble in ether .

The hydrochloride forms a white, crystalline powder, soluble in water, sparingly soluble in alcohol, insoluble in ether and acetone. M. p. 221-223° (from alcohol

Found % C 55.77; H 9.21; N 4.97; Cl 12.46. $C_{13}H_{26}O_3NCl$. Calculated %: C 55.81; H 9.30; N 5.02; Cl 12.72.

Dihydrazide of 3-keto-2,2-di-(carboxyethyl)-quinuclidine (XI). A solution of 0.35 g 3-keto-2,2-di-(β-carbethoxyethyl)-quinuclidine and 0.6 ml hydrazine hydrate in 2 ml anhydrous alcohol was kept at room temperature for 8 days. The alcohol was then taken off in vacuo, the residue was triturated with anhydrous ether, and the crystals were filtered off. Yield 0.2 g colorless, hygroscopic crystals. These were converted to the picrate and the latter was purified by dissolution in acetone and reprecipitation with ether. M. p. 168° (decomp.).

Found %: C 39.93; H 4.00; N 19.70. $C_{13}H_{23}O_3N_5 \cdot 2C_6H_3O_7N_3$. Calculated % C 39.76; H 3.84; N 20.33.

2,2-Di-(β-carbethoxyethyl)-quinuclidine (XII). A solution of sodium ethoxide in alcohol, prepared from 2 g sodium and 50 ml anhydrous alcohol, 2 g 3-keto-2,2-di-(β-carbethoxyethyl)-quinuclidine and 12 ml hydrazine hydrate were heated in a sealed tube at 160-170° for 14 hr. After working up as described for the preparation of 2-(β-carbethoxyethyl)-quinuclidine, 0.9 g 2,2-di-(β-carbethoxyethyl)-quinuclidine was isolated as a colorless, viscous liquid, readily soluble in organic solvents, insoluble in water. B.p. 175-180° (0.2 mm).

Found % C 65.07; H 9.33; N 4.75. $C_{17}H_{29}O_4N$. Calculated %: C 65.52; H 9.26; N 4.50.

Hydrochloride of 2,2-di-(β-carboxyethyl)-quinuclidine (XIII), 0.3 g 3-keto-2,2-di- (β-carbethoxyethyl)-quinuclidine and 5 ml 17% hydrochloric acid were boiled 4 hr. The hydrochloric acid solution was decolorized with carbon and evaporated in vacuo. The residue was triturated with anhydrous acetone. The crystals were filtered and recrystallized twice from a mixture of acetone and a few drops of anhydrous alcohol. Yield 0.1 g colorless crystals, easily soluble in water and alcohol, insoluble in ether, benzene and acetone. M.p. 215-218° (decomp.).

Found % C 53.47; H 7.44; N 5.07; Cl 11.96. $C_{13}H_{22}O_4NCl$. Calculated %: C 53.55; H 7.54; N 4.81; Cl 12.18.

3-Hydroxy-2,2-di-(β-cyanoethyl)-quinuclidine (XIV). To a suspension of 1.2 g lithium aluminum hydride in 20 ml anhydrous ether was added, with stirring, a solution of 1 g 3-keto-2,2-di(β-cyanoethyl)-quinuclidine in 45 ml anhydrous benzene. The reaction mass was heated at 65-70° for 40 hr. This was followed by addition (with cooling) of 3 ml water. The inorganic salts were collected and washed many times with dry pyridine. The pyridine solution was evaporated in vacuo and the dry residue recrystallized from anhydrous alcohol. Yield 0.6 g (59.6%) of colorless crystals, readily soluble in pyridine, chloroform and alcohol, insoluble in ether, benzene, and water.

Found % C 67.44; H 8.32; N 18.02. $C_{13}H_{19}ON_3$. Calculated %: C 67.00; H 8.15; N 18.00.

SUMMARY

Reaction of 3-quinuclidone with acrylonitrile gave a mixture of 3-keto-2-(β -cyanoethyl)-quinuclidine and 3-keto-2,2-di-(β -cyanoethyl)-quinuclidine. Several derivatives of these products were prepared.

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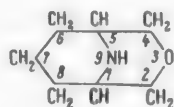

BICYCLIC SYSTEMS ON THE BASIS OF 2,6-LUTIDINE

II. SYNTHESIS OF 3,9-OXAZABICYCLO-[3,3,1]-NONANE AND ITS DERIVATIVES

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In continuation of our work on the synthesis of bicyclic systems starting from 2,6-lutidine, we have obtained a new compound, 3,9-oxazabicyclo-[3,3,1]-nonane.

The starting substance for the synthesis of this bicyclic system was the diethyl ester of dipipecolinic acid, obtained from 2,6-lutidine [1].

Reduction of the latter ester with lithium aluminum hydride in ethereal solution gave 2,6-dihydroxymethyl-piperidine (I).

The latter is readily methylated by a mixture of formic acid and formaldehyde to give 1-methyl-2,6-dihydroxymethylpiperidine (II). The latter can also be prepared by reduction with lithium aluminum hydride of the previously synthesized diethyl ester of N-methyldipipecolinic acid [1]. Treatment with thionyl chloride in chloroform of the hydrochlorides of (I) and (II) gave 2,6-dichloromethylpiperidine (III) and 1-methyl-2,6-dichloromethylpiperidine (IV), respectively. Digestion of 2,6-dihydroxymethylpiperidine with 70% sulfuric acid for 20 hr led to formation of 3,9-oxazabicyclo-[3,3,1]-nonane (V). Attempts to prepare this compound by interaction of 2,6-dichloromethylpiperidine with zinc oxide in an aqueous medium in a tube at 150° did not have the desired results. Pure substances could not be isolated from the resinous product.

3,9-Oxazabicyclo-[3,3,1]-nonane is an extraordinarily volatile crystalline substance; it readily forms salts at the nitrogen on reaction with acid chlorides, but does not enter into the Mannich reaction.
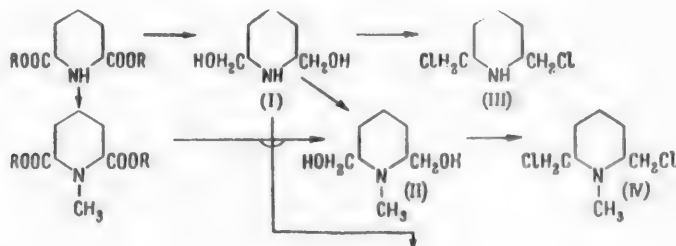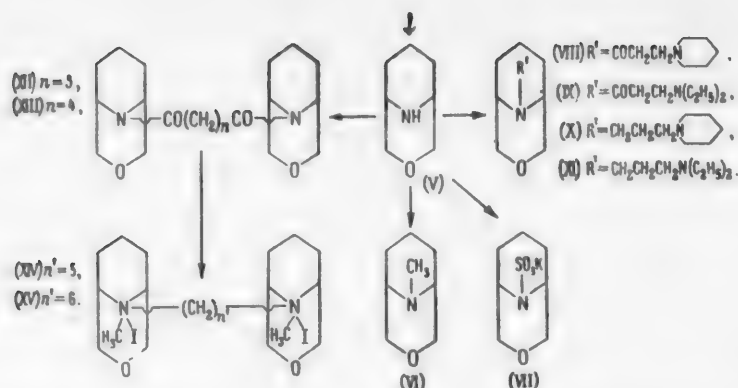
Some N-substituted derivatives of this compound were prepared. Methylation of 3,9-oxazabicyclo-[3,3,1]-nonane with a mixture of formic acid and formaldehyde gave 9-methyl-3,9-oxazabicyclo-[3,3,1]-nonane (VI). Sulfonation with pyridine sulfotrioxide in an aqueous medium gave the N-sulfonic acid, which was isolated as the potassium salt (VII). Sulfonation generally did not take place on heating with pyridine sulfotrioxide in a chloroform medium in tubes. Reaction of 3,9-oxazabicyclo-[3,3,1]-nonane with β-chloropropionyl-chloride in an aqueous alkaline medium followed by boiling of the amide of β-chloropropionic acid with piperidine and diethylamine in anhydrous alcohol gave 9-[β-(N-piperidino)-propionyl]-3,9-oxazabicyclo-[3,3,1]-nonane (VIII) and 9-(β-diethylaminopropionyl)-3,9-oxazabicyclo-[3,3,1]-nonane (IX). The intermediate β-chloropropionamide was not isolated in the pure form and was not analyzed since it is reported in the literature that amides of β-chloropropionic acid, like the acid itself, easily split off hydrogen chloride during distillation to form an unsaturated compound [2]. Reduction of the prepared amides with lithium aluminum hydride in ethereal solution gave 9-[γ-N-piperidino)-propyl]-3,9-oxazabicyclo-[3,3,1]-nonane (X) and 9-(γ-diethylaminopropyl)-3,9-oxazabicyclo-[3,3,1]-nonane (XI). Reaction of excess of 3,9-oxazabicyclo-[3,3,1]-nonane with glutaryl chloride and adipyl chloride in benzene solution in the cold gave the corresponding diamides (XII) and (XIII). The latter were converted to the ditertiary salts (XIV) and (XV) by reduction with lithium aluminum hydride followed by reaction of the resulting amines with methyl iodide.

An experimental study of the prepared compounds, carried out by P. M. Dozortseva, showed that compounds (V) and (VI) exercise a nicotine-like action, and in larger doses show a certain curare-like activity. Compounds (VIII-XI) are less active; in large doses they exert a cytisinolytic action.

EXPERIMENTAL

2,6-Dihydroxymethylpiperidine (I). A solution of 15 g diethyl ester of dipipecolinic acid was added gradually (dropwise) to a suspension of 7.5 g lithium aluminum hydride in 150 ml anhydrous ether. At the close of this operation, the reaction mass was heated for 3 hr at the boil, then cooled to 0-5°; at this temperature 15 ml water was added. The resulting precipitate was filtered and extracted with boiling pyridine. The pyridine extracts were combined, and the pyridine was taken off in vacuo to leave white or faint-yellow crystals which were distilled; b.p. 160° (0.2 mm). White crystals with m.p. 127-129°, soluble in alcohol, chloroform and benzene, sparingly soluble in ether. Yield 7.2 g (76%).

Found % C 57.60; H 10.32; N 9.54. $C_7H_{15}O_2N$. Calculated % C 57.93; H 10.34; N 9.65.

1-Methyl-2,6-dihydroxymethylpiperidine (II). a) A mixture of 8 g 2,6-dihydroxymethylpiperidine, 5.4 g 33.5% formalin, 7.6 g formic acid and 6 ml water was heated 15 hr on a boiling water bath. When the reaction was completed, the cooled mass was treated with excess of 50% potassium carbonate solution and extracted with chloroform. Yield 7.39 g (87.7%) of a colorless, treacly mass with b.p. 131-133° (0.5 mm).

Found % C 59.94; H 10.66; N 8.32. $C_8H_{17}O_2N$. Calculated % C 60.32; H 10.69; N 8.80.

b) A solution of 6.5 g N-methyldipipecolinic acid ester was added dropwise to a suspension of 3.1 g lithium aluminum hydride in 62 ml anhydrous ether. The procedure was the same as described above. The precipitate was extracted with chloroform. Yield 3 g (70%) of a colorless, sticky mass with b.p. 131-133° (0.5 mm).

Found % N 8.34, 8.56. $C_8H_{17}O_2N$. Calculated % N 8.80.

Methoiodide: colorless, lustrous plates with m.p. 238-240° (from alcohol).

Found % N 4.62; I 42.19. $C_9H_{20}O_2NI$. Calculated % N 4.65; I 42.19.

2,6-Dichloromethylpiperidine (III). 3 g 2,6-dihydroxymethylpiperidine was dissolved in anhydrous ethyl alcohol and an alcoholic solution of hydrogen chloride was run in until the mass was acid to Congo. The resulting solution was evaporated to dryness in vacuo. 20 ml of anhydrous chloroform was run into the residue and then 20 ml thionyl chloride was added. The reaction mass was refluxed at 60-70° (bath temperature) for an hour. 2,6-Dichloromethylpiperidine hydrochloride came down and was filtered off and washed with ether. Yield 3.38 g (75%) in the form of white needles, m.p. 258-259° (decomp.).

Found % N 6.40; Cl 48.91. $C_7H_{14}NCl_3$. Calculated % N 6.40; Cl 48.74.

3 g 2,6-dichloromethylpiperidine hydrochloride was dissolved in 5 ml water and excess of 50% potassium carbonate solution (20 ml) was added. An oil separated and was extracted with ether. The ether solution was dried with calcined potassium carbonate, the ether was driven off and the residue was distilled in vacuo to give 1.9 g (76.6%) of substance with b.p. 75-77° (0.5 mm).

Found % N 7.92; Cl 38.85. $C_7H_{13}NCl_2$. Calculated % N 7.68; Cl 39.01.

1-Methyl-2,6-dichloromethylpiperidine (IV). 1.9 g 1-methyl-2,6-dihydroxymethylpiperidine was dissolved in anhydrous ethyl alcohol and acidified with alcoholic hydrogen chloride until acid to Congo. The solution was evaporated in a vacuum and to the treacly residue was added 20 ml anhydrous chloroform, followed gradually (with cooling) by 20 ml thionyl chloride. The reaction mass was heated one hr on a water bath at 60-70°, after which the excess of thionyl chloride and the chloroform were taken off in vacuo. The residual mass was stirred with a small quantity of anhydrous ether and the resulting crystals were filtered off and twice-reprecipitated from anhydrous alcohol with anhydrous ether. Yield 2 g (72.2%) of compound with m.p. 132-134°.

Found % C 41.24; H 6.73; N 6.28; Cl 45.98. $C_8H_{16}NCl_3$. Calculated % C 41.29; H 6.88; N 6.02; Cl 45.80.

3 g 1-methyl-2,6-dichloromethylpiperidine hydrochloride was treated with excess of 50% potassium carbonate solution and extracted with ether; the ethereal extract was dried and the ether driven off. Yield 2.34 g (92.8%) readily mobile, colorless liquid with b.p. 90° (0.2 mm).

Found % C 49.00; H 7.59; N 7.08; Cl 36.61. $C_8H_{15}NCl_2$. Calculated % C 48.98; H 7.65; N 7.14; Cl 36.22.

3,9-Oxazabicyclo-[3,3,1]-nonane (V). A mixture of 5 g 2,6-dihydroxymethylpiperidine, 15 ml concentrated sulfuric acid and 6 ml water was refluxed in a flask for 20 hr. At the end of the reaction, the mass was cooled, diluted with twice the quantity of water, treated with carbon, and filtered. The colorless, transparent solution was cooled to 0-5° and 25% sodium hydroxide solution was added until the liquid was neutral to Congo. The precipitated sodium sulfate was filtered off; the filtrate was made strongly alkaline with 50% potassium carbonate solution (test with phenolphthalein) and extracted with ether. The ether was dried and driven off. The residue was distilled in vacuo. B.p. 100-102° (35 mm). Yield 2.11 g (48.3%). White crystals with m.p. 113-116°, subliming on standing in the air.

Found % C 65.94; H 10.27. $C_7H_{13}ON$. Calculated % C 66.14; H 10.23.

Hydrochloride: white crystals with m.p. 276.5-278.5° (from alcohol).

Found % N 8.62; Cl 21.45. $C_7H_{14}ONCl$. Calculated % N 8.56; Cl 21.71.

Picrate: vivid-yellow crystals with m.p. 191-193°.

Found % C 43.89; H 4.50; $C_{13}H_{16}O_8N_4$ Calculated % C 43.82; H 4.49.

9-Methyl-3,9-oxazabicyclo-[3,3,1]-nonane (VI). 1.06 g 3,9-oxaza-[3,3,1]-nonane, 0.8 g 33.5% formalin, 15 g formic acid and 0.7 ml water were heated on a boiling water bath for 15 hr. At the end of the reaction the mass was treated with excess of 50% potassium carbonate solution and extracted with ether. The ethereal extract was dried, the ether was driven off, and the residue was sublimed at normal pressure. Yield 0.9 g (76.9%). White crystals with m.p. 54-55°.

Found % C 67.83; H 10.68. $C_8H_{15}ON$. Calculated % C 68.08; H 10.63.

Hydrochloride: white crystals with m.p. 261-262° (decomp.)(from anhydrous alcohol).

Found % N 8.08; Cl 19.88. $C_8H_{16}ONCl$. Calculated %: N 7.88; Cl 20.00.

Potassium salt of 3,9-oxazabicyclo-[3,3,1]-nonane-9-sulfonic acid (VII). 1.59 g 3,9-oxazabicyclo-[3,3,1]-nonane was dissolved in 6 ml water; ice was added, followed by 2 g pyridine sulfotrioxide, and the reaction mass was shaken 15 min. Addition was then made of 3.5 g potassium carbonate and the mass was shaken for a further 30 min. with ice cooling. Undissolved potassium carbonate was brought into solution by addition of water, and the resulting solution was filtered and evaporated in a dish. The dry residue was extracted with anhydrous alcohol. The alcoholic solution was evaporated to give 2.04 g (62%) of potassium salt which was recrystallized from alcohol. Heating of the potassium salt in presence of barium chloride and hydrochloric acid led to deposition of barium sulfate.

Found % N 5.45;   12.32; H_2O 6.44. $C_7H_{12}O_4NSK \cdot H_2O$. Calculated % N 5.32; S 12.16; H_2O 6.84.

9-[β-(N-Piperidino)-propionyl]-3,9-oxazabicyclo-[3,3,1]-nonane (VIII) 2 g 3,9-oxazabicyclo-[3,3,1]-nonane was dissolved in 10 ml water and the solution was cooled; simultaneous addition was then made dropwise (with stirring) of 2.2 g β-chloropropionyl chloride and a solution of 0.67 g sodium hydroxide in 1.5 ml water, the temperature of the reaction mass being kept not higher than 5°. At the end of this operation, stirring was continued at the same temperature for another 30 min., after which the cooling was stopped and stirring was carried out until the temperature of the mass rose to 16°. The mass was made alkaline with excess of 50% potassium carbonate solution and extracted with ether; the extract was dried and the ether driven off to leave 2.45 g (71.6%) of technical 9-(β-chloropropionyl)-3,9-oxazabicyclo-[3,3,1]-nonane in the form of a light-yellow oil. This was dissolved in 20 ml anhydrous ethyl alcohol, 1.91 g piperidine was run in, and the mass was boiled 5 hr. The alcohol was then distilled off, the residue was treated with excess of 50% potassium carbonate solution, and the resulting precipitate was extracted with chloroform. The solution was dried and the chloroform was distilled off to leave 2.27 g (75.9%) of 9-[β-(N-piperidino)-propionyl]-3,9-oxazabicyclo-[3,3,1]-nonane. M.p. 83-85°.

Hydrochloride: white crystals with m.p. 241-243° (from alcohol).

Found % N 9.31; Cl 11.81. $C_{15}H_{27}O_2N_2Cl$. Calculated % N 9.25; Cl 11.73.

9-[β-Diethylaminopropionyl]3,9-oxazabicyclo-[3,3,1]-nonane. (IX). 2.35 g diethylamine and 20 ml anhydrous alcohol were heated 5 hr at the boil. Further procedure was as described above. There was obtained 1.7 g (83.7%) of compound with b.p. 135-137° (0.35 mm).

Hydrochloride: white crystals with m.p. 179-180° (reprecipitated from alcohol with ether).

Found % C 57.90; H 9.13; N 9.61; Cl 12.34. $C_{14}H_{27}O_2N_2Cl$. Calculated % C 57.83; H 9.29; N 9.63; Cl 12.22.

9-[γ-(N-Piperidino)-propyl]-3,9-oxazabicyclo-[3,3,1]-nonane (X). 2.25 g 9-[β-(N-piperidino)-propionyl]-3,9-oxazabicyclo-[3,3,1]-nonane was reduced with 0.64 g lithium aluminum hydride in ethereal solution. Yield 1.2 g (56.3%) compound with b.p. 124-126° (0.2 mm).

Dihydrochloride: white, hygroscopic crystals with m.p. 240-242° (decomp.) (reprecipitated from alcohol with ether).

Found % N 8.68, 8.63; Cl 21.45. $C_{15}H_{30}ON_2Cl_2$. Calculated % N 8.61; Cl 21.84.

9-(γ-Diethylaminopropyl)-3,9-oxazabicyclo-[3,3,1]-nonane (XI). 2.73 g 9-(β-diethylaminopropionyl)-3,9-oxazabicyclo-[3,3,1]-nonane was reduced with 0.79 g lithium aluminum hydride in ethereal solution. Yield 1.4 g (54.9%) of compound with b.p. 100-102° (0.2 mm).

Dihydrochloride: white crystals with m.p. 259° (from alcohol).

Found % N 9.06; Cl 22.30. $C_{14}H_{30}ON_2Cl_2$. Calculated % N 8.94; Cl 22.68.

Glutaroyl-bis-[N-(3,9-oxazabicyclo-(3,3,1)-nonane)] (XII). Into a solution of 1.85 g 3,9-oxazabicyclo-[3,3,1]-nonane in 3 ml water at 0° were simultaneously introduced 1.35 g glutaryl chloride and 2.32 g 25%

sodium hydroxide solution. After this operation was completed, the reaction mass was stirred 30 min at $0°$, then treated with excess of 50% potassium carbonate solution and extracted with chloroform. The chloroform extract was dried, the chloroform was distilled off, and the residue was distilled in vacuo to give 1.8 g (70.7%) of compound with b.p. 237-239° (0.25 mm). The compound crystallizes on cooling. M.p. 114-116°. Soluble in chloroform and alcohol, insoluble in water.

Found % C 65.37; H 8.52; N 8.16. $C_{19}H_{30}O_4N_2$. Calculated % C 65.14; H 8.57; N 8.00.

1,5-Bis-[N-(3,9-oxazabicyclo-[3,3,1]-nonano)]-pentane (XIV). 5 g glutaroyl-bis-[N-(3,9-oxazabicyclo-[3,3,1]-nonane] was reduced with 1.65 g lithium aluminum hydride in ether-benzene solution. Yield 4.2 g (91.3%) of a colorless, treacly mass with b.p. 206-208° (4 mm), which crystallized on standing. M.p. 54-56°. Soluble in organic solvents and insoluble in water.

Found % C 70.76; H 10.55; N 8.66. $C_{19}H_{34}O_2N_2$. Calculated % C 70.80; H 10.55; N 8.69.

Dimetholodide: white crystals with m.p. 269-271°.

Found % N 4.59; I 41.48. $C_{21}H_{40}O_2N_2I_2$. Calculated % N 4.62; I 41.91.

Adipoyl-bis[N-(3,9-oxazabicyclo-[3,3,1]-nonane)] (XIII). 5.9 g 3,9-oxazabicyclo-[3,3,1]-nonane and 4.67 g adipyl chloride gave by the above procedure 5.43 g (64.6%) of compound with b.p. 254-255° (0.45 mm). Crystallizes on cooling, m.p. 143-145°. Soluble in chloroform and alcohol, insoluble in water.

Found % C 65.57; H 8.45; N 7.59. $C_{20}H_{32}O_4N_2$. Calculated % C 65.93; H 8.79; N 7.69.

1,5-Bis-[N-(3,9-oxazabicyclo-[3,3,1]-nonano]-hexane (XV). 8.6 g adipoyl-bis-[N-(3,9-oxazabicyclo-[3,3,1]-nonane)] was reduced with 2.7 g lithium aluminum hydride in ether-benzene solution. Yield 6.9 g (87.3%) of colorless, treacly mass with b.p. 251-253° (0.6 mm), crystallizing on cooling. M.p. 32-34°. Soluble in organic solvents, insoluble in water.

Found % C 71.68; H 10.61; N 8.32. $C_{20}H_{36}O_2N_2$. Calculated % C 71.42; H 10.71; N 8.33.

Dimetholodide: white crystals with m.p. 251-253°.

Found % N 4.30; I 40.46. $C_{22}H_{42}O_2N_2I_2$. Calculated % N 4.52; I 40.97.

SUMMARY

1. A new bicyclic compound, 3,9-oxazabicyclo-[3,3,1]-nonane, was synthesized starting from 2,6-lutidine.

2. Several derivatives of 3,9-oxazabicyclo-[3,3,1]-nonane were synthesized with the objective of study of their pharmacological properties.

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THE SYNTHESIS OF 7-MONOSUBSTITUTED 1-AZABICYCLO-
[3,2,1]-OCTANES

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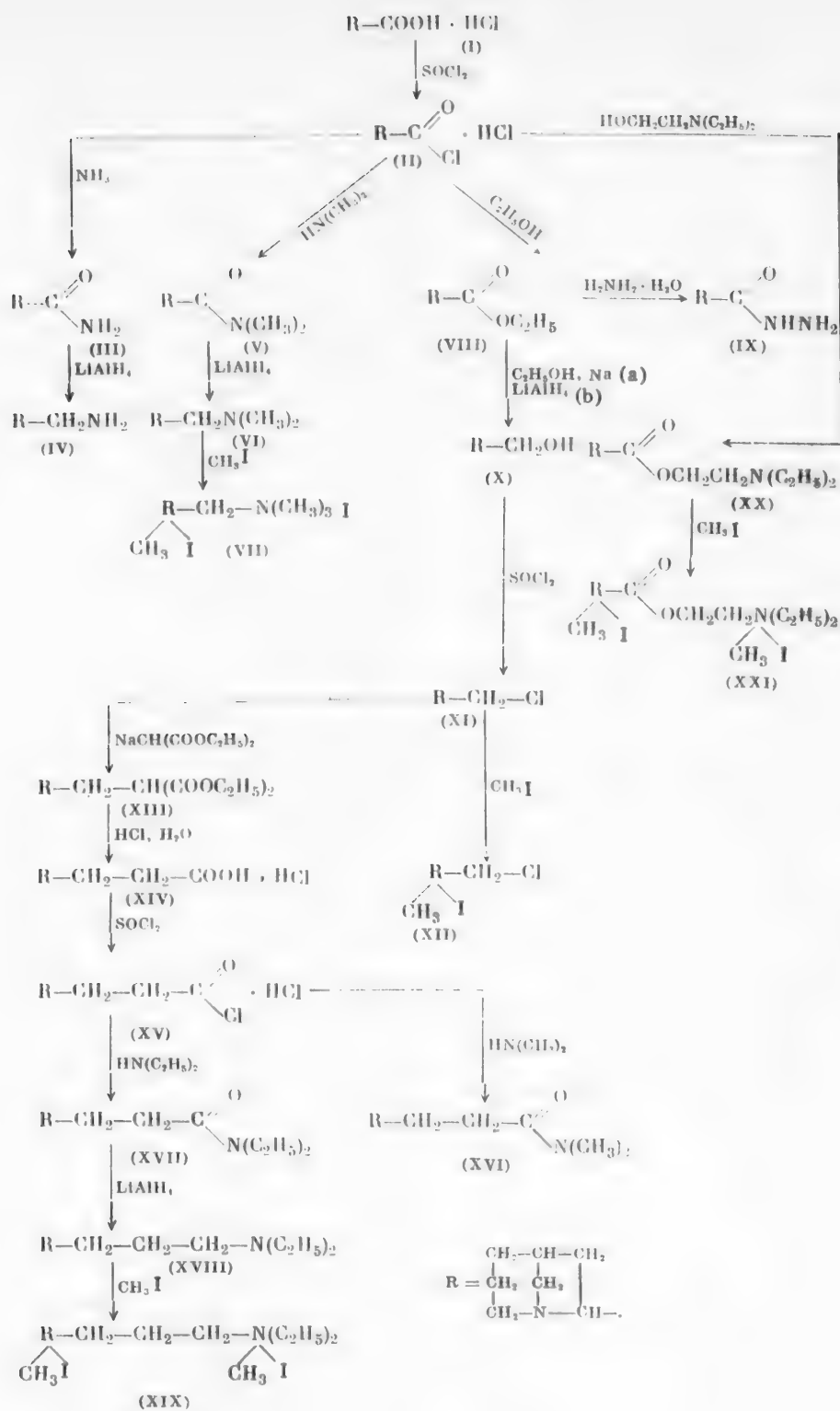Research Institute

In the preceding communication we described the synthesis of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid [1]. The presence of a reactive carboxyl group makes this acid useful for the synthesis of various 7-mono-substituted 1-azabicyclo-[3,2,1]-octanes. The latter are of great interest from the biological aspect since pharmacologically active substances have been found among the isomeric 2-monosubstituted quinuclidines [2].

In the present paper we describe the synthesis of 7-monosubstituted 1-azabicyclo-[3,2,1]-octanes: amides, amines, hydrazides, esters, alcohols, halogenated derivatives, acid chlorides, and some quaternary salts. The starting substance for the preparation of these compounds was 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid (I), which was converted to the acid chloride (II) and subsequently to 7-monosubstituted 1-azabicyclo-[3,2,1]-octanes by the scheme set forth on following page.

Reaction of (II) with ammonia and dimethylamine gives respectively, the amide (III) and the dimethylamide (V), which are reduced by lithium aluminum hydride to the amines (IV) and (VI). Reaction of ethyl alcohol and diethylaminoethanol with the hydrochloride of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid chloride gives the ethyl (VIII) and diethylaminoethyl (XX) esters of the acid. The ethyl ester (VIII) reacts with hydrazine hydrate to form the hydrazide (IX), which can then be reduced by lithium aluminum hydride or sodium in boil-ing alcohol to 7-hydroxymethyl-1-azabicyclo-[3,2,1]-octane (X). Reaction of (X) with thionyl chloride in a chloroform medium leads to 7-chloromethyl-1-azabicyclo-[3,2,1]-octane (XI). Unlike the chlorine atom in the isomeric 2-chloro-methylquinuclidine which has a low reactivity [3], the chlorine atom in 7-chloromethyl-1-azabicyclo-[3,2,1]-octane is extremely mobile. Reaction of (XI) with sodium iodide in anhydrous acetone leads to separation of a certain quantity of sodium chloride, which indicates replacement of the chlorine atom by iodine. Sodium malonic ester acts on (XI) to give 7-(β,β-dicarbethoxyethyl)-1-azabicyclo-[3,2,1]-octane (XII) which on boiling with concentrated hydrochloric acid undergoes hydrolysis and partial decarboxylation to 7-(β-carboxyethyl)-1-azabicyclo-[3,2,1]-octane (XIV).

Starting from (XIV) a series of derivatives were synthesized by transformations similar to those described above on starting from 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid. We prepared the acid chloride of 7-(β-carboxyethyl)-1-azabicyclo-[3,2,1]-octane (XV), and from the latter by treatment with dimethylamine and diethylamine were obtained the dimethylamide (XVI) and diethylamide (XVII) of 7-(β-carboxyethyl)-1-aza-bicyclo-[3,2,1]-octane. Reduction of (XVII) with lithium aluminum hydride yielded 7-(γ-diethylaminopropyl)-1-azabicyclo-[3,2,1]-octane (XVIII).

Treatment of the prepared bases (VI), (XI), (XVIII) and (XX) with methyl iodide transformed them into the corresponding methoiodides (VII), (XII), (XIX) and (XXI). The dimethoiodides of 7-(γ-diethylaminopropyl)-1-azabicyclo-[3,2,1]-octane (XIX) and of the diethylaminoethyl ester of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid (XXI) possess marked blocking action on the ganglion of the autonomic nervous system resembling the ac-tion of dioquin — the dimethoiodide of the diethylaminoethyl ester of quinuclidine-2-carboxylic acid [4] — but rather weaker.

R—COOH · HCl
(I)

| SOCl₂

R—C(=O)Cl · HCl ————— HOCH₂CH₂N(C₂H₅)₂
(II)

NH₃ ↓   HN(CH₃)₂ ↙   C₂H₅OH ↘

R—C(=O)NH₂   R—C(=O)N(CH₃)₂   R—C(=O)OC₂H₅   —H₂NH₂·H₂O→   R—C(=O)NHNH₂
(III)   (V)   (VIII)   (IX)

LiAlH₄ ↓   LiAlH₄ ↓   C₂H₅OH, Na (a)
                                         LiAlH₄ (b)

R—CH₂NH₂   R—CH₂N(CH₃)₂   R—CH₂OH   R—C(=O)OCH₂CH₂N(C₂H₅)₂
(IV)   (VI)   (X)   (XX)

            CH₃I   CH₃I ↓

        R—CH₂—N(CH₃)₃ I   R—C(=O)OCH₂CH₂N(C₂H₅)₂
        | |
        CH₃ I (VII)   CH₃ I
                                                     (XXI)

R—CH₂—Cl ← SOCl₂
(XI)

NaCH(COOC₂H₅)₂ ↓   CH₃I ↓

R—CH₂—CH(COOC₂H₅)₂   R—CH₂—Cl
(XIII) |
                                        CH₃ I
HCl, H₂O ↓   (XII)

R—CH₂—CH₂—COOH · HCl
(XIV)

SOCl₂ ↓

R—CH₂—CH₂—C(=O)Cl · HCl —————————

(XV)   HN(CH₃)₂ ↓

HN(C₂H₅)₂ ↓

R—CH₂—CH₂—C(=O)N(C₂H₅)₂   R—CH₂—CH₂—C(=O)N(CH₃)₂
(XVII)   (XVI)

LiAlH₄ ↓

R—CH₂—CH₂—CH₂—N(C₂H₅)₂
(XVIII)

CH₃I ↓

R—CH₂—CH₂—CH₂—N(C₂H₅)₂
| |
CH₃ I   CH₃ I
(XIX)

R = CH₂—CH—CH₂
     | |
     CH₂   CH₂
     | |
     CH₂—N——CH—

1-Azabicyclo-[3,2,1]-octane-7-carboxylic acid amide (III). 10.5 of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid hydrochloride (I) and 88 g thionyl chloride were heated 3 hr at 60-65°. Unreacted thionyl chloride was distilled off in vacuo; the residue in the form of a white, crystalline powder was the hydrochloride of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid chloride (II). M.p. 265-267° (decomp.). Yield 11.52 g.

11.52 g of the acid chloride was added with vigorous stirring to 200 ml 21.2% aqueous ammonia solution at -5°. After this operation the mass was stirred for another hour at -5° and for an hour at room temperature; the ammoniacal solution was then decolorized with active carbon, saturated with potassium carbonate and repeatedly extracted with chloroform. The extract was dried with potassium carbonate and evaporated in vacuo at 50°. Yield of technically pure amide 5.15 g. Purification was effected by passing a solution of 5.15 g amide in 75 ml chloroform repeatedly through a bed of active carbon until the solution was colorless; the chloroform was then taken off in vacuo. Yield 4.83 g (56.8%) pure compound in the form of a white, crystalline powder, soluble in benzene, chloroform and ethyl alcohol, poorly soluble in ether. M.p. 136.5-138.5°.

Found % N 18.02. $C_8H_{14}ON_2$. Calculated % N 18.17.

7-Aminomethyl-1-azabicyclo-[3,2,1]-octane (IV). A solution of 4.5 g 1-azabicyclo-[3,2,1]-octane (IV). A solution of 4.5 g 1-azabicyclo-[3,2,1]-octane-7-carbo ylic acid amide in 110 ml anhydrous benzene was stirred into a suspension of 2.48 g lithium aluminum hydride in 44 ml absolute ether. The reaction mixture was heated 28 hr at 55-60°. Addition was then made (with cooling) of 4.2 ml water, the mass was stirred 30 min, the benzene-ether solution was filtered and the precipitate was repeatedly washed on the filter with ether and chloroform until the volume of the filtrate was 0.5 liter. The filtrate was dried with potassium carbonate and evaporated in vacuo. The residue was distilled. Yield 2.7 g (66.3%). A colorless oil, readily soluble in benzene, chloroform, ether and water; strongly absorbs carbon dioxide from the air. B.p. 98-100° (13.5 mm), n_D^{20} 1.5028.

Found % C 68.45, 68.50; H 11.27, 11.35. $C_8H_{16}N_2$. Calculated % C 68.60; H 11.43.

1-Azabicyclo-[3,2,1]-octane-7-carboxylic acid dimethylamide (V). 1.9 g hydrochloride of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid chloride was added to a solution(cooled to -10°) of 5.12 g dimethylamine in 55 ml anhydrous ether. The reaction mass was stirred 30 min, 8 ml 50% aqueous potassium carbonate solution was run in, and the mixture was well shaken. The ether layer was separated and the aqueous layer repeatedly extracted with chloroform. The ether-chloroform solution was dried with potassium carbonate and evaporated in vacuo. The residue was distilled. Yield of dimethylamide (V) 1.14 g (69.4%). A colorless oil, soluble in chloroform and ether.

B.p. 120° (1 mm), n_D^{20} 1.5088.

Found % C 65.63; H 9.82; N 15.34, 15.24. $C_{10}H_{18}ON_2$. Calculated % C 65.90; H 9.95; N 15.38.

7-Dimethylaminomethyl-1-azabicyclo-[3,2,1]-octane (VI). A solution of 3.1 g 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid dimethylamide in 41 ml absolute ether was added to a suspension of 1.43 g lithium aluminum hydride in 29 ml absolute ether. The mixture was diluted with 50 ml absolute ether and the reaction was conducted as for preparation of (IV); yield of amine (VI) 1.55 g (54.2%). B.p. 101-101.5° (14-15 mm), n_D^{20} 1.4800. A transparent, colorless oil, soluble in water, alcohol, ether and chloroform.

Dimethoiodide (VII): a white, crystalline powder with m.p. 243-244°, readily soluble in water, moderately soluble in alcohol.

Found % N 6.33. $C_{12}H_{26}N_2I_2$. Calculated % N 6.14.

Ethyl ester of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid (VIII). 80 ml anhydrous alcohol was added to 8.15 g hydrochloride of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid chloride, and the resulting solution was boiled 3 hr. After removal of the alcohol by distillation in vacuo, the residue was treated with 18 ml 50% aqueous potassium carbonate solution; the oil that formed was extracted with ether, and the ethereal solution was dried with potassium carbonate. The ether was taken off in vacuo and the substance was distilled. B.p. 124-125° (12.5 mm). Yield 5.7 g (74.4%). A slightly yellow oil with a strong ammoniacal odor, readily soluble in alcohol and ether.

B.p. 124-125° (12 mm), d_4^{20} 1.0527, n_D^{20} 1.4800, MR_D 49.46; calc. 49.57.

Found %: N 7.39, 7.64. $C_{10}H_{17}O_2N$. Calculated %: N 7.64.

Hydrazide of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid (IX). A solution of 5.03 g ethyl 1-azabicyclo-[3,2,1]-octane-7-carboxylate and 2.7 ml hydrazine hydrate in 6 ml anhydrous alcohol was heated 3 hr at the boil. The alcohol and excess of hydrazine hydrate were distilled off in vacuo and the residue was cooled at -10° for 24 hr. The crystals were triturated with absolute ether, filtered, and dried in a vacuum desiccator. Yield 4.61 g (99%). White crystals, easily soluble in water and alcohol, insoluble in ether. M. p. 93-94.5°.

Found %: C 57.00; H 8.91; N 24.89. $C_8H_{15}ON_3$. Calculated %: C 56.75; H 8.93; N 24.83.

7-Hydroxymethyl-1-azabicyclo-[3,2,1]-octane (X). a) 5.73 g metallic sodium was added to a boiling solution of 5.66 g ethyl 1-azabicyclo-[3,2,1]-octane-7-carboxylate in 57 ml absolute alcohol. After the sodium had dissolved, the reaction mixture was cooled to room temperature, 34 ml water was added, and the alcohol was distilled off in vacuo. The residue was dissolved in a small quantity of water, the alkaline solution was repeatedly extracted with ether, the ethereal solution was dried with potassium carbonate, the solvent was evaporated in vacuo, and the residue was distilled. Yield 1.75 g (40.2%) of the alcohol in the form of a transparent oil, soluble in ether and chloroform.

B.p. 114-115° (13 mm), d_4^{20} 1.0316, n_D^{20} 1.5012, MR_D 40.34; calc. 40.21.

Found %: C 67.84; H 11.13; N 9.85, 9.92. $C_8H_{15}ON$. Calculated %: C 68.04; H 10.71; N 9.92.

b) A solution of 11.6 g ethyl 1-azabicyclo-[3,2,1]-octane-7-carboxylate in 116 ml absolute ether was added with vigorous stirring to a suspension of 5.33 g lithium aluminum hydride in 107 ml absolute ether in the course of 80 min. The mixture was stirred 1 hr at the boiling point of ether, then cooled, and treated with 10 ml water; the inorganic hydroxides were filtered off and thoroughly washed on the filter with ether. The precipitate was stirred with 30 ml 50% aqueous potassium carbonate solution and extracted with ether. The combined ethereal solution was dried with potassium carbonate and evaporated in vacuo, the residue was distilled. Yield 7.88 g (88%).

B.p. 112-113.5° (13 mm), n_D^{20} 1.5032.

Found %: C 68.19; H 10.88; N 9.97. $C_8H_{15}ON$. Calculated %: C 68.04; H 10.69; N 9.93.

7-Chloromethyl-1-azabicyclo-[3,2,1]-octane (XI). 18.3 ml 15% alcoholic hydrogen chloride solution was added to 3.06 g 7-hydroxymethyl-1-azabicyclo-[3,2,1]-octane. Distillation of the alcohol in vacuo left 4.51 g of the hydrochloride of 7-hydroxymethyl-1-azabicyclo-[3,2,1]-octane with m.p. 259-261°. To the latter were added 18 ml chloroform and 18 ml thionyl chloride. The mixture was heated 30 min at 70°, the chloroform and excess of thionyl chloride were taken off in vacuo, the residue was treated with 10.2 ml 50% aqueous potassium carbonate solution, and the chloride base was extracted with ether. The ethereal solution was dried with potassium carbonate, the ether was evaporated in vacuo, and the residue was distilled. Yield 4.1 g (91%) of compound as a colorless, transparent oil, soluble in ether and chloroform. B.p. 101.5° (13 mm), n_D^{20} 1.5011.

Found %: C 60.45; H 8.88; N 9.01. $C_8H_{14}NCl_2$. Calculated %: C 60.18; H 8.84; N 8.77.

Hydrochloride: colorless, extremely hygroscopic crystals, soluble in alcohol, insoluble in ether. M.p. 206-207°.

Found %: C 48.99; H 7.71; N 7.02. $C_8H_{15}NCl_2$. Calculated % C 48.99; H 7.17; N 7.14.

Methoiodide (XII): colorless crystals, easily soluble in water and alcohol, insoluble in ether. M.p. 148-150°.

Found %: I 42.13. $C_9H_{17}NCl I$. Calculated %: I 42.20.

7-(β,β-Dicarbethoxyethyl)-1-azabicyclo-[3,2,1]-octane (XIII). 6.9 g malonic ester was added to a solution of 1 g metallic sodium in 18.6 ml absolute alcohol; this was followed by 6.9 g 7-chloromethyl-1-azabicyclo-[3,2,1]-octane dissolved in 10 ml absolute alcohol. The mixture was heated 20 hr at 100° and cooled; the sodium chloride was filtered off and washed with absolute alcohol. The filtrate was evaporated in vacuo and the residue was distilled; the fraction boiling at 150° (0.3 mm) was collected; n_D^{20} 1.4769. Yield 5.27 g (43.1%). Colorless oil, soluble in acetone and alcohol.

Found %: C 63.28, 63.38; H 8.88; 9.03; N 5.23. $C_{15}H_{25}O_4N$. Calculated % C 63.60; H 8.88; N 4.95.

Hydrochloride of 7-(β-carboxyethyl)-1-azabicyclo-[3,2,1]-octane (XIV). 2.82 g 7-(β,β-dicarbethoxyethyl)-1-azabicyclo-[3,2,1]-octane and 27 ml concentrated hydrochloric acid were heated 10 hr at 140-145°. The hydrochloric acid solution was cooled, decolorized with active carbon and evaporated on a steam bath. The crystals were separated from mother liquor and the latter was treated in the same manner as before to give an additional quantity of crystals. Yield 1.62 g (74.2%). Colorless crystals, soluble in water and alcohol, insoluble in ether. M.p. 252-254°.

Found % C 54.53, 54.95; H 8.18, 8.37; N 5.94. $C_{10}H_{17}O_2N$·HCl. Calculated % C 54.70; H 8.26; N 6.37.

Dimethylamide of 7-(β-carboxyethyl)-1-azabicyclo-[3,2,1]-octane (XVI). 1.31 g hydrochloride of 7-(β carboxyethyl)-1-azabicyclo-[3,2,1]-octane and 6.7 ml thionyl chloride were heated 3 hr at 60°. The excess of thionyl chloride was distilled off in vacuo at 40°. There was obtained 1.55 g of the hydrochloride of 7-(β-carboxyethyl)-1-azabicyclo-[3,2,1]-octane acid chloride (XV) in the form of a yellow, crystalline powder. The latter was added to a solution of 3.84 g dimethylamine in 45 ml ether cooled to -10°, and the mixture was stirred 3 hr at -5°. To the mixture was then added 20 ml 50% aqueous potassium carbonate solution, the ether layer was collected, and the aqueous layer was exhaustively extracted with chloroform. The ether-chloroform solution was dried with potassium carbonate and evaporated in vacuo; the residue was distilled. The fraction boiling at 169-172° (0.5 mm) was collected; n_D^{20} 1.4960. Yield 0.32 g (25.6%). A slightly colored, viscous oil, soluble in ether and chloroform.

Dipicrate: yellow crystals. M.p. 160-162° (from alcohol).

Found % C 43.41, 43.50; H 4.67, 4.53. $C_{12}H_{22}ON_2 \cdot 2C_6H_3O_7N_3$. Calculated % C 43.15; H 4.19.

Diethylamide of 7-(β-carboxyethyl)-1-azabicyclo-[3,2,1]-octane (XVII). 3.33 g 7-(β-carboxyethyl)-1-azabicyclo-[3,2,1]-octane hydrochloride was treated with 17 ml thionyl chloride as described above. The resulting acid chloride was mixed with 10 ml absolute ether, and into the suspension was stirred a solution of 13.4 g diethylamine in 15 ml absolute ether, the temperature being maintained at about 0°. The reaction mass was stirred another 45 min, after which 17 ml 50% potassium carbonate solution was added and the mass was extracted with ether. The ethereal extract was dried with potassium carbonate and evaporated in vacuo, and the residue was distilled. B.p. 137-139° (0.16 mm), n_D^{20} 1.5035. Yield 2.26 g (62.6%). A transparent, viscous oil, soluble in ether and chloroform.

Found % N 11.50, 12.07. $C_{14}H_{26}ON_2$. Calculated %: N 11.76.

7-(γ-Diethylaminopropyl)-1-azabicyclo-[3,2,1]-octane (XVIII). 2.26 g diethylamide of 7-(β-carboxyethyl)-1-azabicyclo-[3,2,1]-octane was dissolved in 23 ml absolute ether and reduced for 25 hr with 0.72 g lithium aluminum hydride in 14 ml absolute ether as described for preparation of (IV) and (VI). To the cooled mixture was added 1.52 ml water; the mass was stirred 20 min and then filtered. The precipitate was washed on the filter with ether. The ethereal solution was dried with potassium carbonate and evaporated in vacuo. The residue was distilled. B.p. 140-142° (6 mm), n_D^{20} 1.4850. Yield 0.78 g (36.7%). A faintly colored oil, soluble in ether. It was identified in the form of the dimethoiodide (XIX), which was prepared by adding 0.3 ml of the base to a solution of 1 ml methyl iodide in 4 ml absolute ether. The precipitate was filtered and dried. White crystals, readily soluble in water and alcohol, insoluble in ether. M.P. 232-234°.

Found % N 5.66. $C_{16}H_{34}N_2I_2$. Calculated % N 5.52.

Diethylaminoethyl ester of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid (XX). 4.39 g hydrochloride of 1-azabicyclo-[3,2,1]-octane-7-carboxylic acid chloride and 98 ml diethylaminoethanol were heated 3 hr at 100°. The excess of diethylaminoethanol was taken off in vacuo at 100°, the residue was treated with 18 ml 50% aqueous potassium carbonate solution and the separated oil was extracted with ether. The ethereal extract was dried with potassium carbonate and evaporated in vacuo, and the residue was distilled. Yield 3.25 g (61.2%). A colorless oil, soluble in ether and alcohol. B.p. 114.5-116.5° (0.15 mm), 154.5-156.5° (4.5 mm).

Found % N 10.69, 10.75. $C_{14}H_{26}O_2N_2$. Calculated % N 11.02.

The dimethoiodide (XXI) was obtained by dissolving 1.76 g of (XX) in 2 ml absolute ether and stirring in 2.06 g methyl iodide in 2 ml absolute ether. The resulting oil gradually crystallized. The crystals were washed on the filter with a little absolute ether and dried in a vacuum desiccator over phosphorus pentoxide. Yield 3.03 g (81.2%). The dimethoiodide is in the form of white, extremely hygroscopic crystals, moderately soluble in acetone, insoluble in ether and alcohol. M.p. 204-206°.

Found % N 4.88, 4.92; I 45.8. $C_{16}H_{32}O_2NI_2$. Calculated % N 5.21; I 47.1.

SUMMARY

A number of 7-monosubstituted 1-azabicyclo-[3,2,1]-octanes were synthesized. It was shown that the halogen atom in 7-chloromethyl-1-azabicyclo-[3,2,1]-octane differs from the halogen in the previously described 2-chloromethylquinuclidine in possessing considerable mobility, thus enabling condensation with sodium malonic ester. Some quaternary salts of 7-monosubstituted 1-azabicyclo-[3,2,1]-octanes exercise a blocking action on the ganglion of the autonomic nervous system.

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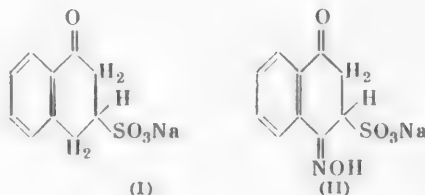
HYDROXY DERIVATIVES OF ANTHRACENE

I. THE BISULFITE COMPOUNDS OF 1-ANTHROL AND 4-NITROSO-1-ANTHROL

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A study of the properties of the bisulfite compounds of 1-naphthol and 4-nitroso-1-naphthol [1,2] enabled the following structures to be proposed (I) and (II):

(I)   (II)

In the present work we investigated the products of addition of bisulfite to 1-anthrol and 4-nitroso-1-anthrol.

The bisulfite compound of 1-anthrol is formed by treatment of 1-anthrol with a boiling solution of sodium bisulfite [3]. There are no data for composition and properties of this compound in the literature. The compound $C_{14}H_{10}OH \cdot NaHSO_3 \cdot 3H_2O$ that we prepared is stable in a neutral and acid medium, but it is easily decomposed by alkalies to form sulfite and 1-anthrol. Treatment with hydroxylamine, semicarbazide and phenylhydrazine in an acetic acid medium gives, respectively, the oxime, semicarbazone and phenylhydrazone of the bisulfite compound of 1-anthrol. This reflects the presence in the bisulfite compound of a free carbonyl group and indicates the structure of 1-oxo-1,2,3,4-tetrahydroanthracene-3-sulfonic acid (III).

The structures of the oxime semicarbazone and phenylhydrazone may be represented by formulas (IV), a, b and c:

(III)   (IV) a, R = OH,
b, R = NHCONH$_2$,
c, R = NHC$_6$H$_5$.
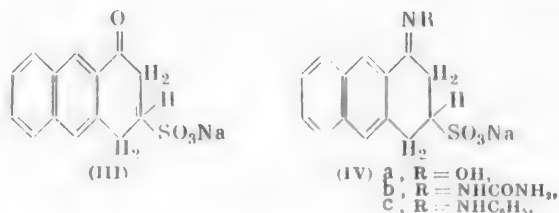
The bisulfite compound of 4-nitroso-1-anthrol was prepared by treatment of 4-nitroso-1-anthrol with sodium bisulfite solution in presence of a little pyridine. In the absence of pyridine the yield falls from 82 to 6%. A similar phenomenon was observed in 1954 when the bisulfite compound of alizarin-3-quinoline was prepared [4].

The bisulfite compound of 4-nitroso-1-anthrol easily loses a molecule of sulfite under the action of caustic alkalies, while with hydroxylamine hydrochloride in presence of sodium acetate it forms the bisulfite compound of 1,4-anthraquinonedioxime. The latter is more resistant to alkalies than the bisulfite compound of 4-nitroso-1-anthrol, but when boiled with sodium hydroxide it breaks down to sulfite and the sodium salt of 1,4-anthraquinonedioxime.

The transition from the bisulfite compound of 4-nitroso-1-anthrol to the bisulfite compound of 1,4-anthra-quinonedioxime points to addition of the bisulfite molecule not to the carbonyl group but at the double carbon-carbon bond (V and VI).
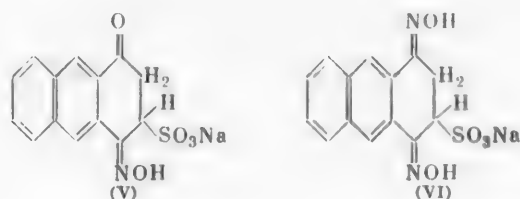
It follows from the results obtained that the bisulfite compounds of 1-anthrol and 4-nitroso-1-anthrol are analogous in structure to the corresponding derivatives of the naphthalene series.

EXPERIMENTAL

Bisulfite compound of 1-anthrol (III). A mixture of 9.7 g 1-anthrol (m.p. 151-152°), 68.9 g 37.8% sodium bisulfite solution and 200 ml water was boiled 20 hr. A very small quantity of precipitate (0.2 g) was filtered off and washed with 50 ml water. To the filtrate was added 100 ml saturated sodium chloride solution. The precipitated bisulfite compound was filtered, washed with 50 ml 10% sodium chloride solution, with alcohol and with ether. The yield of product containing 96.2% bisulfite compound was 15.4 g (84.2%).

For analysis, a weighed sample of the bisulfite compound was dissolved in 100 ml water, the solution was made alkaline with 5 ml 40% sodium hydroxide, diluted after 5 min. with 1500 ml water, and acidified with 10 ml hydrochloric acid (d 1.18). The resulting suspension was titrated with iodine.

The sodium salt forms colorless plates (from water), easily soluble in water and sparingly in alcohol.

Found %: H_2O 14.78 (dried at 120°); C 47.70; H 4.67; Na 6.51, M 353.7 (iodometric determination). $C_{14}H_{11}O_4SNa \cdot 3H_2O$. Calculated %: H_2O 15.34; C 47.72; H 4.86; Na 6.53. M 352.3.

Oxime (IVa). A solution of 17.6 g (III), 4.17 g hydroxylamine hydrochloride and 10 g crystalline sodium acetate in 90 ml water was boiled 30 min. To the slightly colored solution was then added 50 ml saturated barium chloride solution. The barium salt came down on cooling and was filtered and washed with alcohol and ether. Yield 17.5 g. Colorless needles (from water), sparingly soluble in hot water and insoluble in alcohol. The compound does not split off sulfuric acid on treatment with 10% sodium hydroxide at 20° for 12 hr. Boiling of the solution in dilute hydrochloric acid converts the compound into (III) which, after being made alkaline and subsequently reacidified, forms sulfur dioxide and 1-anthrol (m.p. 151-152°).

Found %: H_2O 4.58 (dried at 130°); C 44.34; H 3.61; N 3.60; Ba 18.07. $C_{14}H_{12}O_4NS$ $^1/_2$ Ba $\cdot$ H_2O. Calculated %: H_2O 4.78; C 44.59; H 3.71; N 3.71; Ba 18.22.

Semicarbazone (IVb). A solution of 17.6 g (III), 6.7 g semicarbazide hydrochloride and 50 g crystalline sodium acetate in 120 ml water was heated 30 min at 85°. After cooling, the precipitate was filtered and washed with alcohol and ether. Yield 18.3 g. The sodium salt forms colorless plates (from 50% alcohol), easily soluble in water and sparingly in alcohol. It behaves like the oxime towards acids and alkalies but is slightly decomposed by 10% sodium hydroxide in the course of 12 hr at 20°.

Found %: H_2O 7.30 (dried at 120°); C 47.08; H 4.38; N 10.99; Na 6.05. $C_{15}H_{14}O_4N_3SNa \cdot 1.5 H_2O$. Calculated %: H_2O 7.08; C 47.11; H 4.45; N 10.98; Na 6.02.

Phenylhydrazone (IVc). A solution of 8.65 g phenylhydrazine hydrochloride in 50 ml water was added at 60° to a solution of 17.6 g (III) and 20 g crystalline sodium acetate in 100 ml water. The resulting suspension was cooled to 5°, and the precipitate was filtered and washed with alcohol and ether. Yield of sodium salt of the phenylhydrazone 21.2 g. Yellowish, rectangular plates (from 80% alcohol), easily soluble in water and sparingly in alcohol.

Found %: H_2O 15.76 (dried at 105°); N 5.82; Na 4.91 $C_{20}H_{17}O_3N_2SNa \cdot 4 H_2O$. Calculated %: H_2O 15.65; N 6.08; Na 5.00.

Bisulfite compound of 4-nitroso-1-anthrol (V). 4.46 g 4-nitroso-1-anthrol with m.p. 232° (decomp.) (prepared by the action of sodium nitrite and zinc chloride on 1-anthrol in an alcoholic medium [5]), 11 g 37.8% sodium bisulfite solution, 50 ml water and 0.5 ml pyridine were stirred 8 hr at 55°. The resulting reddish-brown solution was filtered from the small resinous precipitate, the filter was washed with 5 ml hot water, and 13 g sodium chloride was added to the filtrate while the latter was heated. The mixture was cooled to 10° and the precipitate was filtered and washed with alcohol and ether. Yield 95% of sodium salt of bisulfite compound 6.04 g (82%) (the analytical procedure was the same as for III). Colorless needles (from 80% alcohol), very readily soluble in water and sparingly soluble in alcohol. A red solution is formed in dilute alkalies, from which 4-nitroso-1-anthrol is deposited on acidification.

Found % H_2O 6.50 (dried at 105°); C 47.96; H 3.48; N 4.14; Na 6.35. $C_{14}H_{10}O_5NSNa \cdot 1.25 H_2O$. Calculated %: H_2O 6.44; C 48.07; H 3.57; N 4.00; Na 6.58.

Bisulfite compound of 1,4-anthraquinonedioxime (VI). A solution of 4.2 g (V), 1 g hydroxylamine hydrochloride and 2 g crystalline sodium acetate in 20 ml water was boiled 45 min. The small quantity of 4-nitroso-1-anthrol formed (0.09 g) was filtered off and washed with 5 ml hot water. Addition to the filtrate of 5 g sodium chloride brought down a precipitate which was filtered and washed with alcohol and ether (4.05 g). Easily soluble in water, less soluble in alcohol; slowly decomposes in 5% sodium hydroxide solution at 20° and splits off sulfite.

Found % H_2O 11.61 (dried at 105°); N 7.10; Na 5.96. $C_{14}H_{11}O_5N_2SNa \cdot 2.5 H_2O$. Calculated % H_2O 11.62; N 7.23; Na 5.94.

1,4-Anthraquinonedioxime. A solution of 1.94 g (VI) in 50 ml 1.5% sodium hydroxide was boiled 10 min, cooled and poured into 50 ml 3% hydrochloric acid. The gelatinous, yellow precipitate was filtered off, washed with water until neutral, dried and recrystallized from dilute alcohol. Yield 0.73 g (64%). Small yellow needles, soluble in alcohol, glacial acetic and chlorobenzene, difficultly soluble in benzene and chloroform, insoluble in water, ether and carbon tetrachloride. The compound darkens at about 215° and gradually decomposes at 240-250°.

Found % C 70.82; H 4.35. $C_{14}H_{10}O_2N_2$. Calculated % C 70.58; H 4.23.

Diacetyl derivative. 0.238 g 1,4-anthraquinonedioxime was boiled 20 min in 10 ml acetic anhydride. The cooled solution began to deposit elongated, yellow prisms which were filtered and washed. Yield 0.252 g (78%), m.p. 231.5° (decomp.) M.p. 235° (decomp.) after recrystallization from acetic anhydride and glacial acetic acid. Soluble in benzene, chloroform and carbon tetrachloride, poorly soluble in alcohol, insoluble in water, alkalies and ether.

Found %: C 66.94; H 4.33. $C_{18}H_{14}O_4N_2$. Calculated % C 67.07; H 4.38.

SUMMARY

1. The bisulfite compound of 1-anthrol reacts with hydroxylamine, semicarbazide and phenylhydrazine to form respectively, the oxime, semicarbazide and phenylhydrazone of the bisulfite compound of 1-anthrol.

2. 4-Nitroso-1-anthrol reacts with sodium bisulfite to form the bisulfite compound of 4-nitroso-1-anthrol. This is converted by the action of hydroxylamine into the bisulfite compound of 1,4-anthraquinonedioxime.

3. The bisulfite compound of 1-anthrol can be assigned the structure of 1-oxo-1,2,3,4-tetrahydroanthracene-3-sulfonic acid, and the bisulfite compound of 4-nitroso-1-anthrol the structure of 1-oxo-4-hydroxylimino-1,2,3,4-tetrahydroanthracene-3-sulfonic acid.

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*Original Russian pagination. See C. B. translation.

HYDROXY DERIVATIVES OF ANTHRACENE

II. THE BISULFITE COMPOUND OF 1-NITROSO-2-ANTHROL

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It was shown previously [1] that the bisulfite compound of 1-nitroso-2-naphthol reacts with hydroxyl-amine to form the bisulfite compound of 1,2-naphthoquinonedioxime, which in turn is capable of a number of transformations. It was of interest to prepare the bisulfite compound of 1-nitroso-2-anthrol and to establish whether the reactions characteristic of the bisulfite compound of 2-naphthol and its derivatives also took place in the anthracene series.

Fieser [2] obtained a low yield of 1-amino-2-anthrol-4-sulfonic acid on acidifying a bisulfite solution of 1-nitroso-2-anthrol, but he did not isolate the bisulfite compound. We prepared the bisulfite compound of 1-nitroso-2-anthrol in 90% yield by treating 1-nitroso-2-anthrol with double the quantity of sodium bisulfite in presence of pyridine. Addition of the latter, as in the case of 4-nitroso-anthrol [3], increased the yield of bisulfite compound, but part of the compound separated as the pyridine salt.

The bisulfite compound of 1-nitroso-2-anthrol is stable in neutral and acid media, but it is quantitatively broken down by alkalies to sulfite and 1-nitroso-2-anthrol. Reduction of the bisulfite compound of 1-nitroso-2-anthrol with sulfurous acid or tin chloride gives 1-amino-2-anthrol-4-sulfonic acid; reaction with hydroxylamine leads to the bisulfite compound of 1,2-anthraquinonedioxime. Transformation into 1-amino-2-anthrol-4-sulfonic acid on reduction with stannous chloride shows that the sulfo group is in the 4 position in the bisulfite compound of 1-nitroso-2-anthrol, while the formation of the bisulfite compound of 1,2-anthraquinonedioxime testifies to the presence of a free carbonyl group. In the light of these facts we can assign to the bisulfite compound of 1-nitroso-2-anthrol the structure of 2-oxo-1-hydroxylimino-1,2,3,4-tetrahydroanthracene-4-sulfonic acid (I). Two directions of transformation in an alkaline medium characterize the bisulfite compound of 1,2-anthra-quinonedioxime: detachment of a molecule of bisulfite and anhydridization of the orthoquinonedioxime group-ing. Different products can be obtained by varying the reaction conditions. 1,2-Anthraquinonedioxime (III) is formed in dilute (5-6%) sodium hydroxide solution at 50°; boiling with 0.1% sodium carbonate solution gives the bisulfite compound of 1,2-anthra-(3',4')-furazan (IV, basic product) and 1,2-anthra-(3',4')-furazan (V). In boiling sodium hydroxide solution, (III), (IV) and, directly, (II) are transformed into compound (V).

Oxidation with dilute nitric acid leads to facile closure of the ortho-quinone grouping of compounds (II) and (III) to give the furoxan ring. Thus, (III) gives quantitatively 1,2-anthra-(3',4')-furoxan (VI), while (II) gives the bisulfite compound of 1,2-anthra-(3',4')-furoxan (VII) and (VI), as a secondary product.

Comparison of the ultraviolet spectra of 1-nitroso-2-anthrol (III), (V) and (VI) (Fig. 1) with the spectra of their bisulfite compounds (Fig. 2) shows that the bisulfite compounds are mainly distinguished by degeneracy of the absorption maximum in the 300 mμ region which characterizes 1,2-anthraquinone (Fig. 1, curve 5). This effect is evidently due to breakdown of the quinoid structure of the carbon ring carrying the functional group owing to addition of bisulfite at the carbon-carbon double bond.

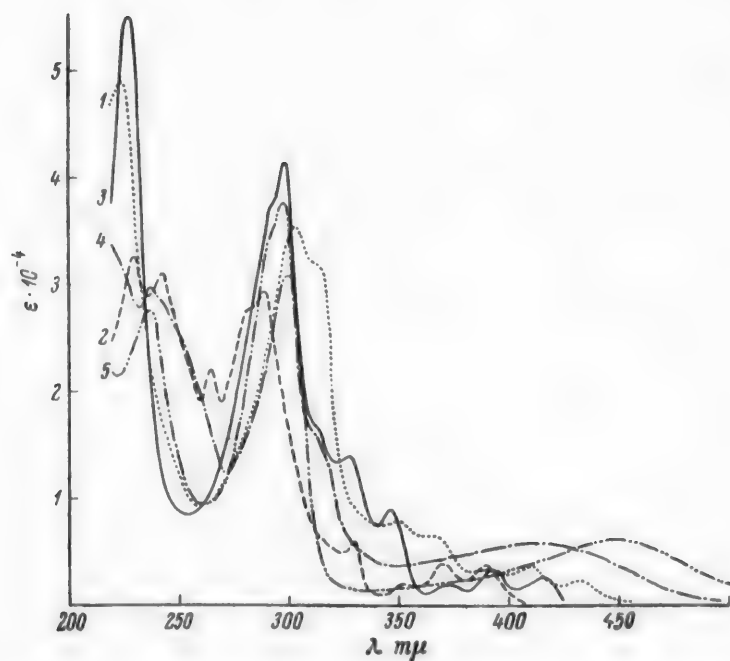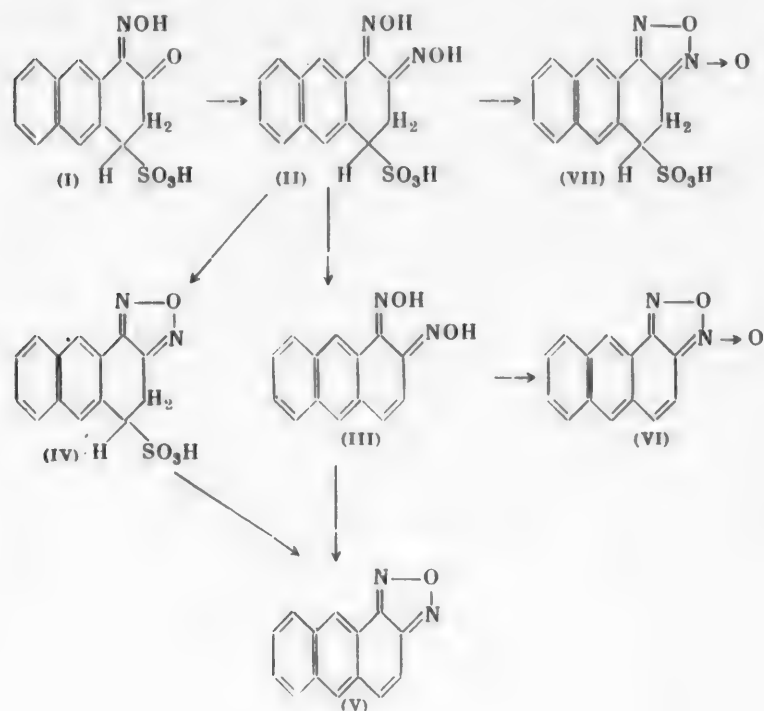# Transformations of the Bisulfite Compound of 1-Nitroso-2-anthrol

Fig. 1. Absorption spectra (in alcohol). 1) 1,2-anthraquinonedioxime (III); 2) 1,2-anthra-(3',4')-furazan (V); 3) 1,2-anthra-(3'4')-furoxan (VI); 4) 1-nitroso-2-anthrol; 5) 1,2-anthraquinone.

The similarity between the chemical properties of the bisulfite compounds of 1-nitroso-2-anthrol and 1,2-anthraquinonedioxime and the properties of the bisulfite compounds of 1-nitroso-2-naphthol and 1,2-naphthoquinonedioxime points to similar structures of these derivatives of the anthracene and naphthalene series.

EXPERIMENTAL

Bisulfite compound of 1-nitroso-2-anthrol (I). a) 2-Anthrol (m.p. 245-247°) was prepared by reducing the sodium salt of 2-anthraquinonesulfonic acid with zinc dust [4] and fusing the reduction product with potassium hydroxide [5]; 2-anthrol was purified by vacuum sublimation.

29.1 g 2-anthrol was nitrosated with sodium nitrite and zinc chloride in an alcoholic medium [5]. There was obtained 30.5 g nitroso compound with m.p. 174° (decomp.); according to the literature 1-nitroso-2-anthrol melts at 188° (decomp.) [5].

A mixture of the pulverized nitroso compound, 71.4 g 39.3% sodium bisulfite solution, 95 ml water and 1.6 ml pyridine was stirred 10 hr at 45-50°. 18 hours after completion of the heating, the mass was filtered. The precipitate was washed on the filter with alcohol and ether and treated with 450 ml water heated to 70°. The undissolved portion was separated and to the orange solution was added 100 g sodium chloride. The precipitated sodium salt of (I) was filtered off and washed with alcohol and ether. Yield 29.5 g The insoluble residue (8.2 g) was again treated with sodium bisulfite. In this manner another 6.4 g of sodium salt of (I) was obtained. Total yield 96.2% (35.9 g) of bisulfite compound (63% calculated on the 2-anthrol).

The sodium salt of (I) forms yellowish, square plates (from water), easily soluble in hot water, poorly soluble in cold water, and very sparingly soluble in alcohol. Alkalies decompose it to sulfite and the yellowish-green sodium salt of 1-nitroso-2-anthrol. It breaks down when heated above 100°.

For analysis, 0.3-0.4 g bisulfite compound was dissolved in 100 ml water, 5 ml 40% sodium hydroxide was added, and after 5 minutes the solution was poured into 1500 ml water. The solution was acidified with 10 ml concentrated hydrochloric acid, and the yellow suspension was titrated with iodine.

Found %: C 46.35; H 3.78; N 4.08; Na 6.48. M 364.7 (iodometric determination). $C_{14}H_{10}O_5NSNa \cdot 2H_2O$. Calculated %: C 46.28; H 3.88; N 3.86; Na 6.33. M 363.3.

b) 30.13 g 1-nitroso-2-anthrol with m.p. 188° (decomp.), prepared by decomposition of (I) with sodium hydroxide, was stirred 5 hr at 50-55° with 71.4 g 38.3% sodium bisulfite solution, 95 ml water and 5 ml pyridine. The reaction mass was worked up as in a). Yield 96.3% of sodium salt (41.64 g or 82% yield reckoned on the 2-anthrol). The "insoluble residue" consisted of 3.21 g (8.1%) of the pyridine salt of (I). The compound forms colorless, rectangular plates, poorly soluble in water; it partially hydrolyzes in hot aqueous solution with release of pyridine; sodium hydroxide decomposes it to the sodium salt of 1-nitroso-2-anthrol, sulfite and pyridine. Does not contain water of crystallization; gradually breaks down when heated in a capillary at above 200°.

Found %: C 59.37; H 4.02. $C_{19}H_{16}O_5N_2S$. Calculated %: C 59.52; H 3.94.

Fig. 2. Absorption spectra of the bisulfite compounds (in alcohol).
1) 1,2-anthraquinonedioxime (II); 2) 1,2-anthra-(3',4')-furazan (IV); 3) 1,2-anthra-(3',4')-furoxan (VII); 4) 1-nitroso-2-anthrol (I), in 80% alcohol.

1-Amino-2-anthrol-4-sulfonic acid. a) A mixture of 1.1 g sodium salt of (I), 1.5 g stannous chloride, 2 ml concentrated hydrochloric acid and 8 ml water was brought to the boil and rapidly cooled. Small grey needles started to come down at about 60°, and hydrogen sulfide came off. The precipitate was filtered, and washed with 10% hydrochloric acid, water, alcohol and ether. Yield 0.8 g. After copper sulfate and sodium nitrite had been added, the suspension of the substance in water formed an orange solution which gave a blue coloration with a sodium carbonate solution of resorcinol. Oxidation of the substance with 20% nitric acid gave the ammonium salt of 1,2-anthraquinone-4-sulfonic acid which formed an orange precipitate with aniline water, while on treatment with methanol and concentrated sulfuric acid it was transformed into 2-methoxy-1,4-anthraquinone with m.p. 215.5-216°. A mixture with 2-methoxy-1,4-anthraquinone prepared by Fieser's method [2] melted at 215.5-216°.

b) To a solution of 1.82 g of sodium salt of (I) in 40 ml water was added 2 ml 37.8% sodium bisulfite solution and 3 ml concentrated sulfuric acid. After standing 14 days in a closed vessel at 20°, the resulting crystals were filtered, washed with water and reprecipitated from 2% sodium sulfite solution. Yield 1.04 g (70%). Small, greenish-yellow needles, insoluble in water and alcohol. The properties of the compound resembled those of the product of method a).

Bisulfite compound of 1,2-anthraquinonedioxime (II). A solution of 54.5 g sodium salt of (I), 11.5 g hydroxylamine hydrochloride and 25 g crystalline sodium acetate in 250 ml water was heated 30 min at 95-98°. 50 g sodium chloride was then added and the mass was stood 20 hr at 15°. The precipitate (51.4 g) was filtered and washed with alcohol and ether. After recrystallization from an equal quantity of water, the yield of sodium salt of (II) was 47.5 g (80%). Colorless plates, very easily soluble in water and sparingly in alcohol. The aqueous solution of the compound gives a brown coloration with ferric chloride.

Found % H_2O 13.57 (dried at 130°); C 42.37; H 4.27; N 7.05; Na 5.86. $C_{14}H_{11}O_5N_2SNa \cdot 3H_2O$.
Calculated % H_2O 13.63; C 42.42; H 4.32; N 7.07; Na 5.80.

Isolation of (II) is unnecessary for the synthesis of compounds (III), (V) and (VII).

1,2-Anthra-(3',4')-furazan (V) A mixture of 2.38 g sodium salt of (II), 3.4 ml 40% sodium hydroxide and 20 ml water was boiled 1 hr. After cooling, the precipitate was filtered, washed with water until neutral, and dried. Yield 1.3 g (98.5%), m p. 175.2-175.7°. Yellowish, hexagonal plates (from acetone), m.p. 176-176.2°. Soluble in acetic acid, poorly soluble in alcohol and benzene, insoluble in water, acids and alkalies. Solutions in organic solvents possess a blue fluorescence. The compound easily sublimes in vacuo at about 150° (5 mm) and is slightly more volatile with steam.

Found % N 12.74. $C_{14}H_8ON_2$. Calculated % N 12.72.

1,2-Anthraquinonedioxime (III). a) 3 ml 40% sodium hydroxide solution was run into a solution of 2.38 g sodium salt of (II) in 20 ml water at 50°. The suspension was stirred 5 min at this temperature , quickly cooled, and poured into a cooled mixture of 6 ml concentrated sulfuric acid and 40 ml water. The precipitate was filtered, washed with water until neutral, and dried. The compound was reprecipitated from 1% sodium hydroxide. Yield 1.07 g (74.5%), m.p. 183° (decomp.). After recrystallization from dilute alcohol, the melting point did not rise. Yellow needles, soluble in dilute alkalies, alcohol and acetic acid, poorly soluble in benzene and chloroform, insoluble in water and ether.

b) A mixture of 2.23 g 1-nitroso-2-anthrol, 2 21 g hydroxylamine hydrochloride, 4 g crystalline sodium acetate, 100 ml alcohol and 10 ml water was boiled 1 hr. The reddish-brown solution was decolorized with carbon, and 80 ml alcohol was distilled off from the filtrate. On cooling there was isolated 1.76 g (74%) 1,2-anthraquinonedioxime with m.p. 182° (decomp.). Compound (V) is formed on boiling with alkali solution; m.p. 175.5-176° (from aqueous acetone).

Found % C 70.56; H 4.08; N 11.68. $C_{14}H_{10}O_2N_2$. Calculated % C 70.58; H 4.23; N 11.76.

Bisulfite compound of 1,2-anthra-(3',4')-furazan (IV). 1.2 ml 1% sodium carbonate solution was run into a boiling solution of the sodium salt of (II) in 9 ml water. A precipitate quickly came down from the darkened solution. Boiling was continued 6 hr, after which a sample of the reaction mass ceased to give a coloration with ferric chloride. At the end of the heating, the mass was diluted with 15 ml water, heated 5 min at 90°, and filtered. The insoluble portion was (V) (m.p. 175-175.5°); yield 0.28 g (10%). Addition of 5 g sodium chloride

to the filtrate led to separation of 3.3 g of sodium salt of (IV)(about 70%). Colorless, rectangular plates (from alcohol), crumbles on drying at above 100°. The compound does not give a coloration with ferric chloride; easily soluble in water, less soluble in alcohol. In presence of alkali it splits off sulfite and changes into (V).

Found %: H_2O 14.33 (dried at 130°); C 51.62; H 2.98; N 8.45; Na 6.13. $C_{14}H_9O_4N_2SNa \cdot 3H_2O$. Calculated %: H_2O 14.29; Na 6.98. $C_{14}H_9O_4N_2SNa$. Calculated %: C 51.85; H 2.79; N 8.64.

1,2-Anthra-(3',4')-furoxan (VI). 4.76 g of (III) was stirred 15 min at 90° with 80 ml 15% nitric acid. After cooling, the precipitate was filtered, washed with water until neutral, and dried at 80°. Yield 4.72 g (quantitative), m.p. 173-174°. Long lemon-yellow needles (from aqueous acetone), m.p. 175.9-176.2°. A mixture with (V) melts at 150°. The compound does not give a coloration with ferric chloride; it is insoluble in water, acids and alkalies, sparingly soluble in alcohol and benzene, more easily soluble in acetone and pyridine. Sublimes in vacuo at 170-180° (5 mm).

Found %: C 71.00; H 3.55; N 11.88. $C_{14}H_8O_2N_2$. Calculated %: C 71.18; H 3.41; N 11.86.

Bisulfite compound of 1,2-anthra-(3',4')-furoxan (VII). A solution of 59.4 g sodium salt of (II) in 300 ml water was poured into 150 ml 40% nitric acid at 60° in the course of 15 min. The mass was heated to 90°, stirred at this temperature 15 min, and filtered from the small quantity of precipitate (1.8 g). Vacuum sublimation of the precipitate at 180-200° (5 mm) followed by recrystallization from acetone gave lemon-yellow needles with m.p. 175.5-176°. A mixture with (VI) melted at 175.5-176°.

To the filtrate was added 100 g sodium chloride; after 20 hours the precipitate was filtered, washed until neutral with 15% sodium chloride solution, then with alcohol and ether, and recrystallized from 3 times the quantity of water. Yield of sodium salt of (VII) 45.2 g (80%). Colorless, rectangular plates (from water), easily soluble in water, poorly soluble in alcohol. The compound is stable in neutral and acid media and does not lose bisulfite when boiled with 15% nitric acid.

Found %: H_2O 9.64 (dried at 130°); C 49.41; H 2.80; N 8.14; Na 6.10. $C_{14}H_9O_5N_2SNa \cdot 2H_2O$. Calculated %: H_2O 9.58; Na 6.11. $C_{14}H_9O_5N_2SNa$. Calculated %: C 49.41; H 2.67; N 8.23.

SPECTROSCOPY

Solutions in alcohol with concentrations of 10^{-4} and $0.25 \cdot 10^{-4}$ mole/liter were used for spectroscopic examination with the SF-4 spectrophotometer at intervals of 5 mμ.

SUMMARY

1. Treatment of the bisulfite compound of 1-nitroso-2-anthrol with hydroxylamine converts it into the bisulfite compound of 1,2-anthraquinonedioxime; reduction with stannous chloride gives 1 amino-2-anthrol-4-sulfonic acid.

2. The structure of the bisulfite compound of 1-nitroso-2-anthrol corresponds to the formula of 2-oxo-1-hydroxylimino-1,2,3,4-tetrahydroanthracene-4-sulfonic acid.

3. Depending on the conditions, the bisulfite compound of 1,2-anthraquinonedioxime is converted in an alkaline medium into 1,2-anthraquinonedioxime, the bisulfite compound of 1,2-anthra-(3',4')-furazan or 1,2-anthra-(3'4')-furazan.

4. Oxidation of 1,2-anthraquinonedioxime and its bisulfite compound with nitric acid gives,respectively, 1,2-anthra-(3',4')-furoxan and the bisulfite compound of 1,2-anthra-(3',4')-furoxan.

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HYDROXY DERIVATIVES OF ANTHRACENE

III. TRANSFORMATIONS OF THE BISULFITE COMPOUND OF 1,2-ANTHRA-(3'4')-FUROXAN

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Investigations in the 1,2-naphtho-(3',4')-furoxan series[1] established that in an alkaline medium the bisulfite compound of 1,2-naphtho-(3',4')-furoxan rearranges to 2-nitro-1-naphthylamine-4-sulfonic acid and 1,2-naphthoquinonedioxime-4-sulfonic acid. The similarity in chemical properties of the bisulfite compounds of hydroxy derivatives of anthracene and naphthalene [2,3] led one to expect that the bisulfite compound of 1,2-anthra-(3',4')-furoxan would behave similarly.

Experiments indeed showed that the bisulfite compound of 1,2-anthra-(3',4')-furoxan (I) is converted by alkali into 2-nitro-1-anthramine-4-sulfonic acid (II), 1,2-anthraquinonedioxime-4-sulfonic acid (III) and 1,2-anthra-(3',4')- furoxan (IV). The yield of each compound is markedly dependent on the conditions. Boiling 1% sodium carbonate solution converts (I) into 90% (II), about 4% (IV) and only a trace of (III); on the other hand, in boiling 4% sodium hydroxide solution, the yield of (II) does not exceed 18-20%, the yield of (IV) is 3-4%, and the main product is (III). In an alkaline medium sulfonic acids (II) and (III) easily undergo further transformations to form, respectively, 2-nitro-1-anthrol-4-sulfonic acid (V) and 1,2-anthra-(3',4')-furazan-4-sulfonic acid (VI). Compound (II) can therefore be isolated from sodium carbonate solution only after short-period boiling, and (III) can be isolated from sodium hydroxide solution only at low temperature.

The sulfonic acid (II) is diazotized by nitrosylsulfuric acid, and analysis shows that one nitro group is present. For determination of the relative positions of the amino and nitro groups, the sulfo group was eliminated by hydrolysys with 50% sulfuric acid and the 2-nitro-1-anthramine was converted to 2-nitro-1-anthrol by boiling with sodium hydroxide. Reduction of 2-nitro-1-anthrol with stannous chloride gave 2-amino-1-anthrol, whose triacetyl derivative was found to be identical with the triacetyl derivative of the aminoanthrol prepared from 2-nitroso-1-anthrol [4]. With the objective of establishing the position of the sulfo group, (V) was treated with stannous chloride and the amino compound was oxidized with chromic acid. The resulting 1,2-anthraquinone-4-sulfonic acid was converted to 2-methoxy-1,4-anthraquinone, which was found to be identical with the 2-methoxy-1,4-anthraquinone synthesized from 1,2-anthraquinone by Fieser's method [5].

Reduction of (II) with tin chloride leads to 1,2-anthradiamine-4-sulfonic acid; oxidation of the latter with selenium dioxide gives 1,2-anthra-(3',4')- selenodiazole-4-sulfonic acid. The analogous synthesis of 1,2-anthra-(3',4')-selenodiazole-4-sulfonic acid from (III) is proof of the orientation of the functional groups in the latter compound. The presence of the orthoquinonedioxime grouping is confirmed by the ability of (III) to give a coloration with ferric chloride, to change under the action of alkalies or dehydrating agents (acetic anhydride) into 1,2-anthra-(3',4')-furazan-4-sulfonic acid (VI), and to change on oxidation with nitric acid into 1,2-anthra-(3',4')-furoxan-4-sulfonic acid.

The structure of (III), (VI) and 1,2-anthra-(3',4')-furoxan-4-sulfonic acid is also confirmed by their ultraviolet absorption spectra (Fig. 1) which are similar to those of 1,2-anthraquinonedioxime, 1,2-anthra-(3',4')-furazan and 1,2-anthra-(3',4')-furoxan [3] respectively. The influence of the sulfo group is reflected in the lower intensity of absorption and in the displacement of the maxima by several millimicrons towards the longer

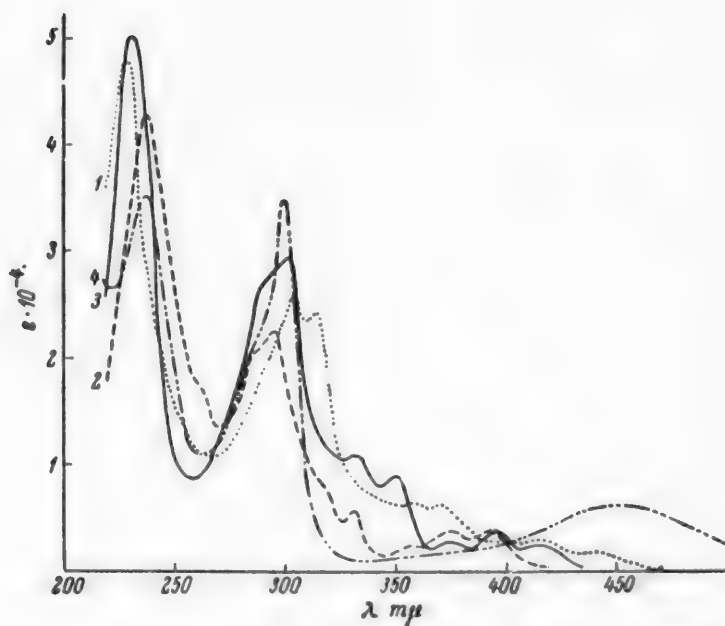Scheme of Transformations of the Bisulfite Compound of 1,2-Anthra-(3',4')-Furoxan in an Alkaline Medium
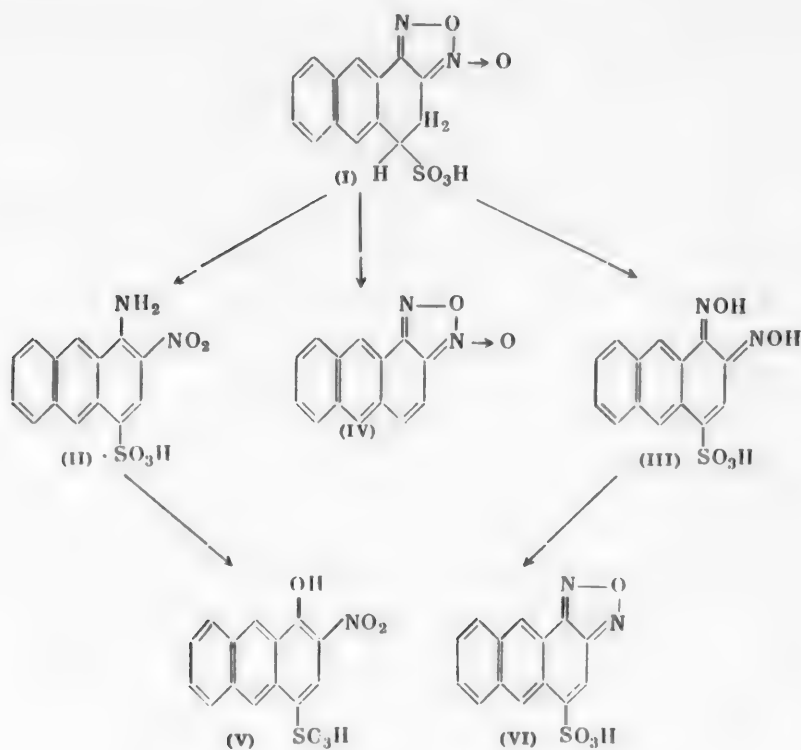

Fig. 1. Absorption spectra (in alcohol). 1) 1,2-anthraquinonedioxime-4-sulfonic acid (III); 2) 1,2-anthra-(3',4')-furazan-4-sulfonic acid (VI); 3) 1,2-anthra-(3',4')-furoxan-4-sulfonic acid; 4) 1,2-anthraquinone-4-sulfonic acid.

waves. Common to the spectra of all of the above-mentioned compounds is the strong absorption maximum at about 300 mμ, which is characteristic of 1,2-anthraquinone [3] and 1,2-anthraquinone-4-sulfonic acid (Fig. 1, curve 4). The second group of compounds — 2-nitro-1-anthramine, 2-nitro-1-anthrol and the corresponding 4-sulfonic acids (Fig. 2) — are distinguished by a different pattern of absorption curves; the introduction of the sulfo group here heightens the intensity of absorption and causes a very slight shift of the maximum towards the shorter waves. We may assume, on the basis of the spectrographic data, that the compounds of the 1st group (Fig. 1) possess the quinoid-ring structure while the compounds of the 2nd group (Fig. 2) retain the anthracene structure. *
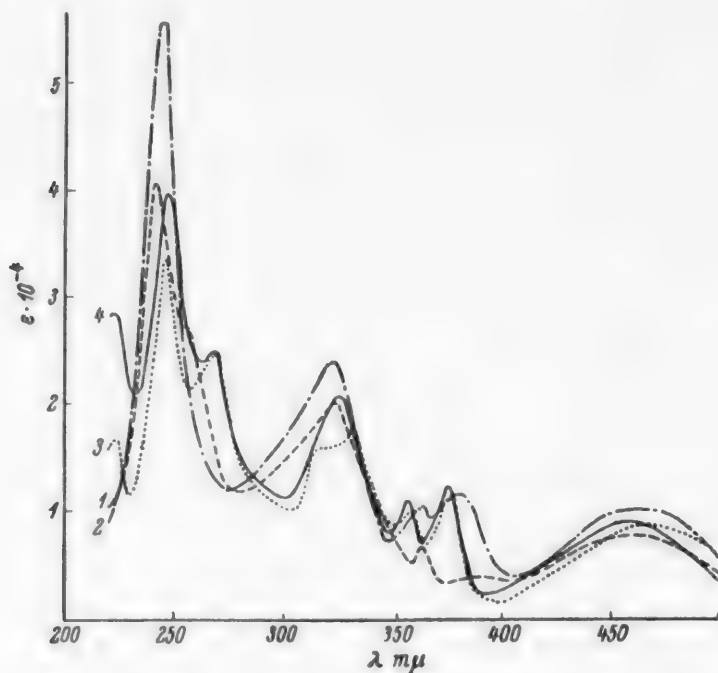

Fig. 2. Absorption spectra in alcohol. 1) 2-nitro-1-anthrol; 2) 2-nitro-1-anthrol-4-sulfonic acid (V); 3) 2-nitro-1-anthramine; 4) 2-nitro-1-anthramine-4-sulfonic acid (II).

Formation of 2-nitro-1-anthramine-4-sulfonic acid (II) from the bisulfite compound of 1,2-anthra-(3',4')-furoxan (I) shows that the oxygen atom which is not common to the nitrogen atoms of the furoxan ring is attached to the nitrogen linked to the second carbon atom of the anthracene ring   Since the position of this oxygen atom in 1,2-anthra-(3',4')-furoxan itself has not been established, formula (IV) is used arbitrarily.

EXPERIMENTAL

2-Nitro-1-anthramine-4-sulfonic acid (II).   10 ml 10% sodium carbonate was rapidly run into a boiling solution of 15.04 g sodium salt of (I) in 90 ml water, and the mass was cooled to 25° in the course of 2 min. 25 g sodium chloride was then added; after cooling to 0°, the precipitate was filtered and washed with 50 ml 10% sodium chloride solution and then with alcohol and ether (10.9 g, precipitate a). The filtrate and the first 20 ml of washings were boiled 1.5 hr, and the cooled, yellowish-grey substance was filtered (0.52 g, precipitate b). After acidification of the solution with hydrochloric acid, a dark-red precipitate came down (1.12 g, precipitate c).

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* The authors thank E. S. Levina and L. G. Lumer for assistance in measurement and analysis of the ultraviolet spectra.

Precipitate a), containing (by analysis) 9.25 of(65.3%) of amino compound, was dissolved in 5% hydro-chloric acid and filtered from the small brownish-yellow residue (0.48 g, precipitate d). Crystals came down when the hydrochloric acid solution was cooled, and they were filtered and dried in vacuo over potassium hydro-xide at 50°. Yield of sulfonic acid (II) 8.04 g (56.8%).

For analysis, 0.4-0.5 g amino compound was dissolved in 250 ml water and the solution boiled with 25 ml 40% sodium hydroxide until ammonia ceased to distil off (the ammonia was trapped in acid). The sodium salt of (V) was isolated after acidification of the alkaline solution.

Addition of sodium nitrite to a solution of (II) in concentrated sulfuric acid led to formation of 1-diazo-2-nitroanthracene-4-sulfonic acid which came down as a dark-grey precipitate when the solution was poured on-to ice. The diazo compound is poorly soluble in water, does not couple with 2-naphthol-3,6-disulfonic acid, but gives a red coloration with resorcinol in sodium carbonate solution Treatment with sodium carbonate converts it into 1-diazo-2-anthrol-4-sulfonic acid, which slowly couples with resorcinol to form a blue dye.

Sulfonic acid (II) forms slender, orange needles (from a mixture of alcohol and hydrochloric acid),soluble in water and alcohol. It breaks down at above 100°; it loses its water of crystallization over phosphorus pen-toxide, turning brown in the process; the original color is restored on standing in the air.

Found %: C 47.63; H 4.08; N 7.79; S 9.03. M 353.9 (from determination of ammonia lost), 363.4 (vanadometrically) $C_{14}H_{10}O_5N_2S \cdot 2H_2O$. Calculated %: C 47.41; H 3.98; N 7.91; S 9.05. M 354.3.

The ammonium salt is obtained by treating the free sulfonic acid with ammonium chloride. Orange-red, bronzing needles (from water), sparingly soluble in alcohol.

Found %: H_2O 5.30 (dried at 130°); N 11.92. $C_{14}H_{13}O_5N_3S \cdot H_2O$. Calculated %: H_2O 5.08; N 11.89.

Recrystallization of precipitate b) from water (with addition of a drop of 40% sodium hydroxide) gave 0.23 g sodium salt of the sulfonic acid (light-yellow needles). Sulfochloride with m.p. 193.5-194° (from benzene); a mixture with the sulfochloride from (VI)has m.p 193.5-194°.

Precipitate c) was recrystallized from ammonium chloride solution and from water; there was obtained 0.72 g of ammonium salt of (V).

Sublimation of precipitate d) at 170-190° (4 mm) gave 0.4 g (4.2%) of a yellow substance; needles (from acetone), m.p. 175.6-176; m.p. of mixture with (IV) 175.5-176°. 1,2-Anthra-(3',4')-furazan was not detected on fractional vacuum sublimation.

2-Nitro-1-anthrol-4-sulfonic acid (V). A solution of 3.763 g sodium salt of (I) in 200 ml water was boiled 1 hr with 20 ml 10% sodium carbonate solution. Addition was then made of 20 ml 40% sodium hydroxide and boiling was continued until ammonia ceased to distil off. The quantity of ammonia corresponded to the formation of 90.2% of (V). A few milligrams of crystalline substance came over with the ammonia and was identified as impure 1,2-anthra-(3',4')-furazan with m.p. 167-168°; a mixture with 1,2-anthra-(3',4')-furazan melts at 170-170.5°; a mixture with (IV) melts at 149-150°. After completion of the boiling, the solution was filtered; vacuum sublimation of the water-insoluble residue (0.12 g) gave 0.09 g of (IV). The filtrate was acidified with hydrochloric acid; the precipitate (3.35 g) was filtered, washed with alcohol and ether,and recrystallized from water. Yield of monosodium salt of (V) 3.13 g (83%). Fine, bright-red, small needles, sparingly soluble in cold water and alcohol.

Found %: H_2O 9.26 (dried at 130°); N 3.69; Na 6.03. M 377.8 (titanometric determination). $C_{14}H_8O_6NSNa \cdot 2H_2O$. Calculated %: H_2O 9.54; N 3.71; Na 6.10. M 377.3.

The disodium salt of (V) was isolated on recrystallization of the monosodium salt from dilute sodium hydroxide solution; long, claret-red needles, very easily soluble in water; changes into the monosodium salt on washing with alcohol or a sodium chloride solution.

The ammonium salt of (V) (prepared from the sodium salt) forms slender, small, orange-red needles (from water), sparingly soluble in alcohol.

Found %: H_2O 10.00; N 7.74. $C_{14}H_{12}O_6N_2S \cdot 2H_2O$ Calculated %: H_2O 9.67; N 7.52.

2-Nitro-1-anthramine.   4.5 g (II) was stirred 5 hr at 115° in 130 ml 50% sulfuric acid. The mass was cooled, poured into 100 ml water and filtered   The precipitate was boiled with 150 ml 1% ammonia solution, filtered, and washed with hot water   Cooling of the ammoniacal filtrate and the aqueous washings led to separation of 1.2 g   ammonium salt of (II) (26.7%). The water-insoluble residue (1.74 g) was heated with 170 ml glacial acetic acid, and the boiling solution was filtered and poured into water. Yield 1.37 g (61.7% calculated on reacted sulfonic acid), m p. 224-225°. Sublimation at 200° (5 mm) gave bright-red, elongated prisms with m p. 231-231.5° , insoluble in water, poorly soluble in alcohol and benzene, more soluble in chlorobenzene and glacial acetic acid.

Found % C 70.54; H 3.98; N 12.09 $C_{14}H_{10}O_2N_2$. Calculated % C 70.58; H 4.23; N 11.76.

2-Nitro-1-anthrol. A mixture of 0.4 g 2-nitro-1-anthramine and 250 ml 7% sodium hydroxide was boiled 4 hr. The quantity of ammonia split off corresponded to formation of 90% hydroxy compound. The solution, whose volume during boiling was maintained at about 200 ml, was filtered hot, and the residue was washed on the filter with 150 ml hot water. To the filtrate and wash liquors was added 40% sodium hydroxide solution; the resulting small, dark-red needles of sodium salt of 2-nitro-1-anthrol were filtered and treated with dilute acetic acid. Yield 0.33 g (82.3%), m.p. 199-199.5°. Sublimation at 180° (5 mm) gave long, red prisms with m.p. 200.5-201°. Insoluble in water, poorly soluble in alcohol; dissolves on heating in dilute alkalies and in glacial acetic acid.

Found % C 70.38; H 3.69; N 5.98. $C_{14}H_9O_3N$. Calculated % C 70.29; H 3.79; N 5.85.

Triacetyl-2-amino-1-anthrol. A mixture of 0.2 g 2-nitro-1-anthrol, 10 ml water, 1 g stannous chloride and 3 ml concentrated hydrochloric acid was boiled one hour. The pale-yellow suspension was poured into 50 ml water and heated to 85-90°.   The solution was filtered; to the filtrate was added 20 ml concentrated hydrochloric acid, and the precipitated hydrochloride of 2-amino-1-anthrol (needles) was filtered off. A mixture of the dried compound, 0.2 g fused sodium acetate and 4 ml acetic anhydride was boiled 15 min and poured into water. The precipitate was collected, dried, and again treated with acetic anhydride. Yield 0.12 g. Greenish, rhombic plates (from alcohol), m.p. 161-162°. Triacetyl-2-amino-1-anthrol prepared from 2-nitroso-1-anthrol [4] had m.p. 160.5-161.5° (from alcohol); a mixture of the two substances melted at 161-162° (according to the literature [4], triacetyl-2-amino-1-anthrol melts at 161°).

1,2-Anthraquinone-4-sulfonic acid and 2-methoxy-1,4-anthraquinone. A mixture of 1.1 g sodium salt of (V), 25 ml water, 5 g stannous chloride and 6 ml concentrated hydrochloric acid was boiled 20 min. After cooling, the precipitate was filtered, washed with water and stirred with 60 ml water. To the suspension was added 20 g ice and 5 ml 10% chromic acid solution. After an hour, 20 g ammonium chloride   was added, and the precipitate was filtered and dissolved in 50 ml warm water. After decolorization of the solution with carbon, the red ammonium salt of 1,2-anthraquinone-4-sulfonic acid was again brought down with ammonium chloride. Yield 0.25 g.   The compound was converted to 2-methoxy-1,4-anthraquinone by Fieser's method [5] — treatment with methanol and concentrated sulfuric acid. Small yellow needles (from alcohol), m.p. 216.5-217°. For the purpose of comparison, 1,2-anthraquinone-4-sulfonic acid was prepared from 1,2-anthraquinone [2] and likewise transformed into 2-methoxy-1,4-anthraquinone; a mixture of both specimens of 2-methoxy-1,4-anthraquinone melted at 216.5-217° (literature [5]: m.p. 217°).

1,2-Anthraquinonedioxime-4-sulfonic acid (III). A mixture of 15.04 g sodium salt of (I), 90 ml water and 20 ml 40% sodium hydroxide was stirred 4 hr at 10-15°. The brownish-yellow precipitate (0.44 g) was filtered and washed with water; when sublimed at 170° (4 mm) it gave 0.36 g (3.8%) of (IV) with m.p. 174-174.5°. To the filtrate and to the first 10 ml of wash water were added 12 ml acetic acid and 20 g sodium chloride. After cooling for 20 hr at 5°, the mass was filtered and the precipitate washed with 50 ml 10% sodium chloride solution and 10 ml water; it was then dried in a vacuum-desiccator over sulfuric acid. Recrystallization from water gave 7.52 g (52.7%) of sodium salt of (III). Orange-yellow needles (from water), easily soluble in alkalies and poorly soluble in alcohol; gives a brown coloration with ferric chloride solution.

Found % H_2O 9.86 (dried at 130°); C 44.69; H 3.63; N 7.25. $C_{14}H_9O_5N_2SNa \cdot 2H_2O$. Calculated % H_2O 9.57; C 44.68; H 3.48; N 7.44.

The filtrate from the recrystallization liquor was evaporated down and the residue recrystallized from water to give 1.4 g (10%) sodium   salt of (VI).

1,2-Anthra-(3',4')-furazan-4-sulfonic acid (VI). a) A mixture of 1.13 g sodium salt of (III) and 8 ml 5% solution of sodium hydroxide was heated 1 hr at 80°. The suspension became lighter in color, and a sample of reaction mass acidified with acetic acid ceased to give a coloration with ferric chloride. After cooling, the precipitate was filtered and washed with alcohol and ether. Yield of sodium salt of (VI) 0.95 g (90%). Long, light-yellow needles (from water), poorly soluble in alcohol.

Found % H_2O 7.53 (dried at 130°); C 48.03, H 3.05; N 7.89. $C_{14}H_7O_4N_2SNa \cdot 1.5H_2O$. Calculated % H_2O 7.74; C 48.14; H 2.86; N 8.02.

Sulfochloride. A mixture of 1 g dried sodium salt of (VI) with the threefold quantity of phosphorus penta-chloride was heated 1 hr at 110°, and the sulfochloride was separated by dilution of the mass with iced water. Yield 0.85 g. Yellow, elongated prisms (from benzene), soluble in alcohol and chloroform; m.p. 193.8-194.3°.

Found % N 9.04; Cl 10.98. $C_{14}H_7O_3N_2SCl$. Calculated % N 8.79; Cl 11.12.

b) A suspension of 1.13 g sodium salt of (III) in 15 ml acetic anhydride was boiled 2.5 hr. On cooling, the precipitate (which had a lighter color) was filtered and washed with alcohol and ether; it was treated with 30 ml boiling water, and the hot solution was filtered. From the filtrate (after partial evaporation) was isolated 0.64 g (61%) sodium salt of (VI). The insoluble residue was washed with cold water and recrystallized from 200 ml water. Yellow plates (0.2 g), insoluble in organic solvents. The compound was not investigated.

c) A solution of 3.763 g (I) in 200 ml water was boiled 2 hr with 20 ml 40% sodium hydroxide. The quantity of ammonia that came off corresponded to the formation of 18.5% of (V). At the conclusion of boiling, the alkaline solution was filtered and the residue washed on the filter with water. Vacuum sublimation of the residue gave 0.09 g (IV); acidification of the filtrate with hydrochloric acid gave 3.2 g of an orange-red mixture of substances. This mixture was dissolved in warm, very dilute sodium hydroxide and the yellow substance was separated by addition of sodium chloride; acidification of the filtrate then gave the red substance. The latter was repeatedly subjected to the same treatment. There was isolated 2.13 g (61%) of the yellow sodium salt of (VI) (sulfochloride), m.p. 193-194° and 0.36 g (10%) red sodium salt of (V) (2-methoxy-1,4-anthraquinone, m.p. 216-216.5°).

1,2-Anthra-(3',4')-furoxan-4-sulfonic acid. Into a suspension of 2.26 g sodium salt of (III) in 14 ml water at 60° was poured 5 ml 55.7% nitric acid, and the mass was stirred 10 min at 90°. 4 g of sodium chloride was then introduced, and the cooled precipitate was filtered, washed to neutrality with 15% sodium chloride solu-tion, and then washed with alcohol and ether. Recrystallization from a 25-fold quantity of water gave 1.58 g (72%) sodium salt of 1,2-anthra-(3'4')-furoxan-4-sulfonic acid. Elongated, yellow plates, poorly soluble in alcohol.

Found % H_2O 7.58 (dried at 120°); C 46.11; H 2.55; N7.46. $C_{14}H_7O_5N_2SNa \cdot 1.5 H_2O$. Calculated % H_2O 7.40; C 46.03; H 2.74; N 7.67.

1,2-Anthradiamine-4-sulfonic acid. a) Into a suspension of 2.26 g sodium salt of (III) in 40 ml water at 70° was poured a solution of 8 g stannous chloride in 12 ml concentrated hydrochloric acid, and the mass was gently boiled 15 min. After cooling, the precipitate (1.53 g) was filtered off, washed with water, alcohol and ether, and reprecipitated from sodium sulfite solution. Yield 1.3 g (75%). Fine yellow plates, insoluble in water and alcohol; the solutions in alkalies rapidly turn brown when heated.

Found % N 9.53; S 11.24 . $C_{14}H_{12}O_3N_2S$. Calculated % N 9.72; S 11.12.

b) 1.06 g compound (II) in 25 ml water was reduced with 4 g stannous chloride in presence of 6 ml hydro-chloric acid by the procedure used for (III). Yield of purified product 0.62 g (72%).

1,2-Anthra-(3',4')-selenodiazole-4-sulfonic acid. Into a suspension of 0.8 g 1,2-anthradiamine-4-sulfonic acid in 20 ml water, heated to 60°, was run a solution of 1 g selenium dioxide in 10 ml water. The mixture was made alkaline with 10 ml 40% sodium hydroxide and the precipitate was filtered, washed with alcohol and ether and recrystallized from water Yield 0.96 g (75%). Long, light-yellow needles, fairly difficultly soluble in water.

Found % H_2O 15.55 (dried at 150°) C 36.60; H 3.14; N 6.00. $C_{14}H_7O_3N_2SSeNa \cdot 4H_2O$. Calculated % H_2O 15.76; C 36.77; H 3.28; N 6.13.

Sulfochloride. A mixture of 0.286 g dried sodium salt of 1,2-anthra-(3', 4')-selenodiazole-4-sulfonic acid and 1 g phosphorus pentachloride was kept 3 hr at 60° and 48 hr at room temperature; it was then diluted with iced water. The precipitate was filtered off, washed with iced water, alcohol and ether, and recrystallized from nitrobenzene. Yield 0.203 g (70%). Yellow, tetragonal and hexagonal prisms, fairly easily soluble in nitrobenzene, less easily in benzene and alcohol. The compound prepared from (III) had m.p. 253° (with decomp.); that prepared from (II) had m.p. 252.5° (decomp.); a mixture of the two substances melted at 253° (decomp.).

Found %: N 7.35; Cl 9.36. $C_{14}H_7O_2N_3SSeCl$. Calculated %: N 7.51; Cl 9.29.

SPECTROSCOPY

Solutions with concentrations of 10^{-4} and $0.25 \cdot 10^{-4}$ mole/liter were used. Measurements were made with the SF-4 spectrophotometer at intervals of 5 mμ.

SUMMARY

1. In presence of alkalies, the bisulfite compound of 1,2-anthrafuroxan rearranges to 2-nitro-1-anthramine-4-sulfonic acid and 1,2-anthraquinonedioxime-4-sulfonic acid. The former is the main product of reaction in sodium carbonate medium; the second is the main reaction product in sodium hydroxide.

2. 2-Nitro-1-anthramine-4-sulfonic acid is converted by hot 50% sulfuric acid into 2-nitro-1-anthramine; alkalies convert it to 2-nitro-1-anthrol-4-sulfonic acid; stannous chloride reduction leads to 1,2-anthradiamine-4-sulfonic acid. The latter is oxidized by selenium dioxide to 1,2-anthra-(3',4')-selenodiazole-4-sulfonic acid.

3. Oxidation of 1,2-anthraquinonedioxime-4-sulfonic acid with nitric acid yields 1,2-anthra-(3',4')-furoxan-4-sulfonic acid; alkalies or acetic anhydride convert the former into 1,2-anthra-(3',4')-furazan-4-sulfonic acid; reduction with stannous chloride leads to 1,2-anthradiamine-4-sulfonic acid.

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THE CONDENSATION OF TRIAMINOPYRIDO [2,3-d]THIAZOLE
WITH CARBOXYLIC ACIDS

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In the preceding work we described the synthesis of 2,5,6-triaminopyrido[2,3-d]thiazole (A) and the products of its condensation with α-dicarbonyl compounds [1]. The objective of the present work was to prepare the products of condensation of 2,5,6-triaminopyrido[2,3-d]thiazole with carboxylic acids.

Condensation of o-diamino derivatives of the aromatic and heterocyclic series with carboxylic acids leads to formation of compounds containing the imidazole ring. It is well known that the amino group in the 3 position of pyridine reacts more readily than the amino group in the 2 position; we could therefore assume that condensation of 2,5,6-triaminopyrido[2,3-d]thiazole (A) with carboxylic acids would lead to derivatives of imidazo[5,6-d] pyrido [2,3-d]thiazole of structure B.
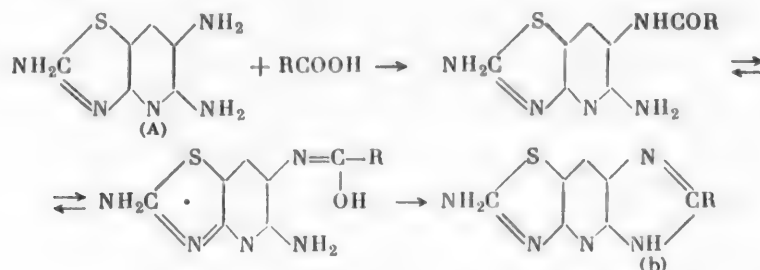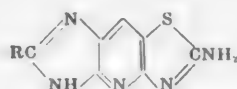

The resulting tricyclic condensed heterocyclic system contains the imidazole nucleus. At the present time various condensed heterocyclic systems containing pyrazine and imidazole rings are engaging the attention of chemists. Imidazo[4,5-b]pyridazines [2], imidazo[4,5-b]pyrazines [3], etc. have been described in the literature. The imidazopyridothiazoles reported in the present work were previously unknown.

In 1928 Phillips [4] proposed a convenient method of preparation of benzimidazole derivatives, consisting in heating of o-phenylenediamine with aliphatic carboxylic acids in solution in 4 N hydrochloric acid for 45 min. Aromatic acids do not enter into the condensation reactions under these conditions. B. A. Poral-Koshits and co-workers showed [5] that hydrochloric acid catalyzes the closure of the imidazole ring. By heating o-phenylenediamine with carboxylic acids in dilute hydrochloric acid at 180° in sealed tubes, these authors succeeded in bringing aromatic carboxylic acids into reaction and in obtaining the corresponding benzimidazole derivatives in good yields. It was recently found that polyphosphoric acid is a good condensing medium which enables the preparation not only of 2-alkyl but also of 2-aryl derivatives of benzimidazole in very good yields [6].

By heating 2,5,6-triaminopyrido [2,3-d] thiazole with aliphatic carboxylic acids in 15% hydrochloric acid for 2-3 hr, it is possible to obtain the corresponding alkyl derivatives of imidazo[5,6-d]pyrido[2,3-d]thiazole. Benzoic, mandelic and phenylacetic acids do not undergo condensation under these conditions.

$$RC \underset{NH}{\overset{N}{\diagdown}} \underset{N}{\diagup} \underset{N}{\overset{S}{\diagdown}} CNH_2$$

Preparation No.	R	Yield (%)	Empirical formula	Sulfur (%) found	calculated	λ (mμ) maximum	minimum
(I)	H	61	$C_7H_5N_5S$	16.74, 16.55	16.75	224, 246, 270–278, 323	237, 263, 287
(II)	CH_3	90	$C_9H_7N_5S \cdot H_2O$	14.34, 14.16	14.35	224, 246—253, 270—275, 326	238, 263, 289
(III)	CH_3CH_2	61	$C_9H_9N_5S$	14.51, 14.53	14.61	225, 247—253, 326	233, 263, 290
(IV)	$CH_3CH_2CH_2$	77	$C_{10}H_{11}N_5S$	14.09	13.73	225, 293, 384	272, 320 *
(V)	$\dfrac{CH_3}{CH_3}\!\!>\!\!CH$	35	$C_{10}H_{11}N_5S$	13.34	13.73	223, 277, 330	263, 290
(VI)	$CH_3CH(OH)$	71	$C_9H_9ON_5S$	13.46, 13.59	13.61	225, 250, 275, 327	249, 264, 289
(VII)	CH_2OH	68	$C_8H_7ON_5S$	14.01, 14.07	14.48	223, 247, 275, 328	249, 265, 289
(VIII)	ONa	70	$C_7H_4ON_5SNa$ **	14.25, 14.31	13.91	224, 274, 334	257, 295
(IX)	SH	90	$C_7H_5N_5S_2$	28.02, 28.30	28.70	223, 252, 353	238, 300

* The hydrochloride was used for obtaining the absorption curve.

** % Calculated: Na 10.04. Found % Na 9.63, 9.76.

Heating of 2,5,6-triaminopyrido[2,3-d]thiazole with benzoic or phenylacetic acid in 15% hydrochloric acid at 180° in sealed tubes failed to give products of condensation. Hydrogen sulfide was detected when the tubes were opened, which indicates partial decomposition of the thiazole ring under these conditions.

We similarly failed to isolate condensation products when 2,5,6-triamino-pyrido[2,3-d]thiazole was heated to 240° with benzoic or phenylacetic acid in a medium of polyphosphoric acid for 4 hr.

The prepared derivatives of imidazo [5,6-d][pyrido 2,3-d] thiazole are listed in the table in which are set forth the yields, analyses, and maxima and minima of the ultraviolet absorption curves. Measurements were made with the SF-4 spectrophotometer.

Fusion of 2,5,6-triaminopyrido[2,3-d]thiazole with urea gave 2-amino-6-hydroxy-imidazo[5,6-d]pyrido [2,3-d]thiazole (VIII) (see table). Heating of triaminopyridothiazole with carbon disulfide in an alcoholic medium led to formation of 2-amino-6-mercapto-imidazo[5,6-d]pyrido[2,3-d]thiazole (IX) (see table).

Derivatives of imidazopyridothiazole are high-melting, crystalline substances, in this respect resembling the derivatives of 2-aminopyrazino[5,6-b]pyrido[2,3-d]-thiazole [1]. They differ from the latter in being more easily soluble in water. Difficulties also arise in the elemental analysis of imidazopyridothiazole derivatives, and only Carius analyses for sulfur give satisfactory results.

Aqueous and alcoholic solutions of imidazo [5,6-d]pyrido[2,3-d]thiazole derivatives fluoresce in light. The solutions darken on standing and form dark-colored precipitates.

EXPERIMENTAL

The starting 2,5,6-triaminopyrido[2,3-d]thiazole has been described previously [1].

2-Amino-imidazo[5,6-d]pyrido[2,3-d]thiazole (I). a) 0.54 g 2,5,6-triaminopyrido[2,3-d]thiazole was boiled 2 hr in 5 ml 80% formic acid. The excess of formic acid was taken off in the vacuum of a water-jet pump during heating on a water bath. The dry residue was suspended in water, treated with aqueous ammonia solution until alkaline, filtered, washed with water, alcohol and ether, and dried. Weight of precipitate 0.4 g. Colorless needles, not melting on heating to 360° (after recrystallization from water). The aqueous and alcoholic solutions fluoresce in light.

Preparation (II) was similarly obtained by boiling triaminopyridothiazole with excess of acetic acid.

b) A mixture containing 0.54 g 2,5,6-triaminopyrido[2,3-d]thiazole, 0.5 ml 80% formic acid and 20 ml 15% hydrochloric acid was boiled 2 hr. The colored solution was decolorized with carbon, and the filtrate was neutralized with ammonia solution. The resulting precipitate was filtered and washed with water, alcohol and ether. Weight of precipitate 0.32 g. It was recrystallized from water. Colorless needles whose analysis and absorption curve fully identified it with the preparation obtained by method a).

Preparations II to VII were similarly obtained by boiling of 0.54 g (0.003 mole) 2,5,6-triaminopyrido[2,3-d]thiazole in 20 ml 15% hydrochloric acid with 0.004 mole acetic, propionic, butyric, isobutyric, lactic and glycolic acids (see table). The products of condensation with butyric and isobutyric acids crystallize badly from water and alcohol since solutions of the free bases darken on standing and deposit dark-colored solids. For analysis they were purified by recrystallization of the hydrochlorides from dilute hydrochloric acid, and the free bases isolated from these salts were recrystallized once from water.

2-Amino-6-hydroxy-imidazo[5,6-d]thiazole (VIII). A well-triturated mixture of 0.54 g triaminopyrido-thiazole and 0.5 g urea was heated on a paraffin-wax bath at 130-140° for 30 min. The initial liquid mass later solidified. After cooling, it was triturated with 2% sodium hydroxide solution and treated with carbon. The colorless filtrate was acidified with 2% acetic acid solution and treated with carbon. The colorless filtrate was acidified with 2% acetic acid solution. The yellow, amorphous precipitate was filtered, and washed with water, alcohol and ether. Yield quantitative. The product does not melt when heated to 320°. For analysis it was recrystallized from 2% sodium hydroxide solution. Red, colorless needles of the sodium salt came down and were filtered, thoroughly washed with water, and dried. Weight 0.45 g.

2-Amino-6-mercapto-imidazo[5,6-d]pyrido[2,3-d]thiazole (IX). A mixture of 0.36 g 2,5,6-triamino-pyrido[2,3-d]thiazole, 0.5 ml carbon disulfide and 20 ml 70% alcohol was boiled 6 hr on a water bath. After only 20-30 minutes' heating, a precipitate commenced to come down. It was filtered, washed with alcohol and ether and dried. Weight 0.4 g. Insoluble in water and alcohol, soluble in dilute alkalies. It was purified by recrystallization from ethylene glycol.

SUMMARY

A number of derivatives of imidazo[5,6-d]pyrido[2,3-d]thiazole were prepared by condensation of 2,5,6-triaminopyrido[2,3-d]thiazole with aliphatic carboxylic acids, urea and carbon disulfide.

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THE REACTION OF ACETOPHENONE WITH AMMONIA IN THE GAS
PHASE IN THE PRESENCE OF TITANIUM VANADATE

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When aldehydes and ketones react with ammonia in the presence of a dehydrating catalyst, condensation reactions often take place, leading to the formation of various pyridine bases which are difficult to prepare by other methods. Chichibabin [1] was the first to observe reactions of this type. Together with Panyutin, Orochko and others [2,3] he obtained 2,4,6-trimethylpyridine from a mixture of acetaldehyde, acetone and ammonia in the presence of alumina, and 2,6-dimethyl-4-phenylpyridine and a number of other pyridine derivatives from acetone and benzaldehyde.

Later, similar condensations were described by other investigators [4,5]; in particular, it is indicated [6] that 2,4,6-trimethylpyridine can be obtained from acetone and ammonia.

By analogy with the preparation of trimethylpyridine from acetone and ammonia, it would be expected that the ammonolysis of acetophenone would lead to the formation of 2,4,6-triphenylpyridine. The object of the present work was to show the possibility of this reaction taking place Fused vanadium titanate, which, as previously established [7], has quite good dehydrating properties, was used as the catalyst.

The results of the first experiments on the ammonolysis of acetophenone showed that the main reaction product in this case is, in fact, 2,4,6-triphenylpyridine. The maximum yield was obtained with a feed of 130 g of catalyst per liter of acetophenone over a period of 1 hour, a 5-10-fold excess of ammonia above the theoretical and a contact time of about 6 seconds.

As may be seen from Fig. 1, which gives the results of one of the series of experiments carried out under these conditions, the yield of 2,4,6-triphenylpyridine at 370-380° was 35% of the initial acetophenone introduced and up to 98% of the reacted acetophenone. At 400° and above, its yield decreased as the result of cracking reactions which were accompanied by the formation of low-molecular products. In the experiments carried out at temperatures below 350° it was found that tarry products were deposited on the surface of the catalyst, as a result of which its activity was reduced. It was established that in this case the activity of the catalyst can be fully restored by injecting air at temperatures of the order of 400°.

EXPERIMENTAL

The reaction was carried out in an apparatus of the throughflow type, previously described [7]. The catalyst was prepared by fusing titanium dioxide and vanadium pentoxide in amounts corresponding to the formula $Ti(VO_3)_4$. The initial acetophenone had an m.p. of 19.5° a b.p. of 198° (690 mm), d_4^{20} 1.024, n_D^{20} 1.5341. The ammonia was fed to the reactor from a cylinder, its rate of feed being regulated by a rheometer.

The reaction products were collected in a 2-liter flask, well cooled with ice, connected to a reflux condenser. After the completion of the experiment the oily layer was separated from the aqueous layer, washed with a 5% solution of alkali and with distilled water. The product obtained was dried over calcined sodium sulfate and the unreacted acetophenone was distilled from it. The b.p. was 197-198° (690 mm), n_D^{20} 1.5344. After recrystallization from boiling ethyl alcohol the undistilled residue, 2,4,6-triphenylpyridine, had an m.p. of 138-139°.
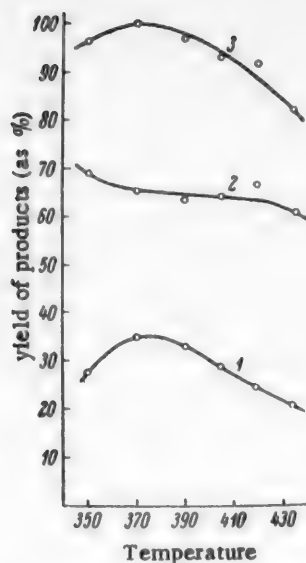
Fig. 1. The ammonolysis of aceto-
phenone in the presence of titanium
vanadate catalyst:
1) 2,4,6-triphenylpyridine; 2)
acetophenone; 3) sum of the reac-
tion products.

Found %: C 89.87; H 5.66; N 4.97. $C_{23}H_{17}N$. Calculated %: C 89.90; H 5.53; N 4.56.

Triphenylpyridine picrate melted at 190°.

To prove the structure of the product obtained, pure 2,4,6-tri-phenylpyridine was prepared in accordance with literature data [8, 9]. The product obtained had an m.p. of 138°. Its picrate melted at 190°.

A mixed melt of the synthesized 2,4,6-triphenylpyridine and the product obtained by ammonolysis melted at 138°. A mixed melt of the picrates of both samples of 2,4,6-triphenylpyridine also showed no depression of the melting point.

SUMMARY

The reaction of the vapor-phase ammonolysis of acetophenone in the presence of titanium vanadate catalyst at 350-435° was investigated. The main product of this reaction is 2,4,6-triphenylpyridine which under optimum conditions is obtained with a yield of up to 35% of the acetophenone fed to the reactor and up to 98% of the reacted acetophenone.

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THE OXIDATION OF ORGANIC COMPOUNDS

XIX. THE LIQUID-PHASE CATALYTIC OXIDATION OF p-XYLENE BY MOLECULAR OXYGEN

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The oxidation of alkylbenzenes by molecular oxygen is one of the most convenient methods of synthesizing valuable oxygen-containing aromatic compounds. At the present time, acetophenone and methylphenylcarbinol are obtained from ethylbenzene [1], cumene hydroperoxide from cumene [2], p-tert -butylbenzoic acid from p-tert -butyltoluene [3], etc., by this method.

In recent years particular attention has been paid to the development of an analogous method for the synthesis of tetraphthalic acid from p-xylene. The most economical method was found to be a four-stage process [4]. However, in spite of the fact that the liquid-phase catalytic oxidation of p-xylene was studied by many investigators [5-8] and that there is a description of a technological system of the process in literature [4], certain problems concerning the reaction mechanism remain obscure. In particular, the reaction mechanism of the catalyst was not studied, the relationship between the reaction velocity and the yield of the oxidation products and the concentration of the catalyst was not investigated and no data are available on the character and order of the oxidative conversions of p-xylene itself, etc. The object of this investigation was to clarify some of these problems.

By means of initial experiments it was established that without a catalyst the oxidation of p-xylene takes place extremely slowly, negligible quantities of aromatic acids being formed. The oxidation also takes place very slowly in the presence of cobalt acetate at a temperature below 130°. All the experiments subsequently described were, therefore, carried out with a catalyst at $133-35°$.

Fig. 1 gives the results of two series of experiments with 0.1% cobalt acetate, carried out in order to study the influence of the duration of the experiment on the process of the oxidation of p-xylene. As may be seen from Fig. 1, in both series of experiments the main direction of the reaction was the incomplete oxidation of p-xylene, accompanied by the formation of aromatic acids, regardless of the amount of catalyst. The maximum yield of aromatic acids was 60%
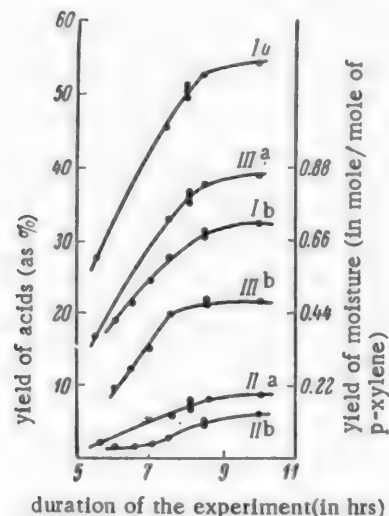

duration of the experiment(in hrs)

Fig. 1. The influence of the duration of the experiment on the process of the oxidation of p-xylene in the presence of 0.1% (a) and 1% (b) cobalt acetate:
I) p- toluic acid; II) terephthalic acid; III) water.

(calculated on the p-xylene taken) and the amount of moisture liberated approximately corresponded to the equation

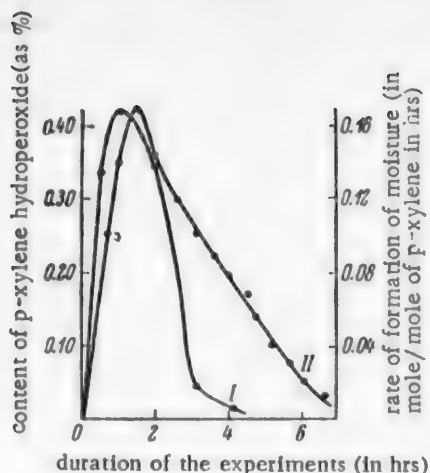$$R-CH_3 + 1^1/_2 O_2 \rightarrow R-COOH + H_2O.$$

Fig. 2. Rate of formation of moisture and the content of p-xylene hydroperoxide during the oxidation of p-xylene in the presence of 0.1% cobalt acetate: I) p-xylene hydroperoxide; II) water.

The main reaction product was p-toluic acid. In the experiments with 0.1% cobalt acetate the yield of this compound was 53.5% (on the p-xylene taken). When 1% of this catalyst was used, the yield of p-toluic acid was somewhat less. With increasing duration of the experiments, the ratio between the yields of p-toluic and terephthalic acids decreased. This indicates that the rate of conversion of p-toluic acid to terephthalic acid increased in the course of time. In spite of this, however, even 8-10 hours after the commencement of the experiment not more than 5-8% terephthalic acid was obtained.

Small amounts of phenols, formaldehyde and carbon dioxide were obtained; the yield of the two latter did not exceed 0.02-0.05 mole per mole of initial substance taken.

The oxidation of p-xylene did not take place uniformly. Observations of the moisture liberated during the reaction show that oxidation took place with spontaneous acceleration in the first 1-1.5 hours. 90-120 minutes after the commencement of the experiment the velocity of the reaction had reached a maximum, after which it gradually decreased. To illustrate what has been said, Fig. 2 shows the results of determinations of the rate of liberation of moisture in one of the experiments with 0.1% cobalt acetate. This diagram also shows the variation of the content of peroxide compounds during the experiment. It is characteristic that the maximum formation of peroxides also takes place during the second hour after the commencement of the experiments.

From the data given it is seen that the liberation of moisture ceased almost completely 7-8 hours after the commencement of the experiment. By this time the content of acids in the reaction mixture had reached a maximum and the reaction had almost finished. The amount of catalyst did not have an appreciable influence on the duration of the process but it did affect the yield of acids.

It should be noted that although the majority of investigators suggest the use of cobalt catalyst (in the form of salts of organic acids) for the liquid-phase oxidation of p-xylene. the data of various authors on the optimum amount of this substance differ markedly. Very varied amounts are recommended, from 0.002 to 1% metal, calculated on the p-xylene taken [9-11].

With the object of a more detailed investigation of the influence of the concentration of catalyst on the process of the oxidation of p-xylene, we carried out experiments in which the amount of cobalt acetate introduced varied from 0.001 to 3% The results of these experiments, given in Fig. 3 and Table 1, show that the variation of the amount of catalyst is reflected primarily on the velocity of the reaction. The maximum rate of oxidation of p-xylene was recorded with 0.1% catalyst. The maximum yield of acids was obtained in the same experiments. With decreasing or increasing amount of catalyst, the reaction velocity and the yield of acids decreased. A similar relationship is shown in the ratio of p-phthalic and terephthalic acids which characterizes the extent of oxidation of the p-xylene. With an increasing amount of catalyst from 0.006%, the relative content of terephthalic acid increased and reached a maximum with 1% cobalt acetate (at the same time the ratio of the yields of p-toluic and terephthalic acids was 5.8-6.2). In experiments with 3% catalyst, however, the oxidation of p-toluic acid to terephthalic acid took place extremely slowly and the ratio between the yields of the acids was the same as with 0.01% cobalt acetate.

An association of a different character is found between the amount of catalyst and the duration of the induction period. The inverse relationship applying in the given instance was preserved throughout the entire range of the investigated concentrations of the catalyst. The induction period, which with low amounts of cobalt acetate is very long, gradually decreased with increasing concentration of catalyst, and in the experiments with 1-3% catalyst it was practically absent.
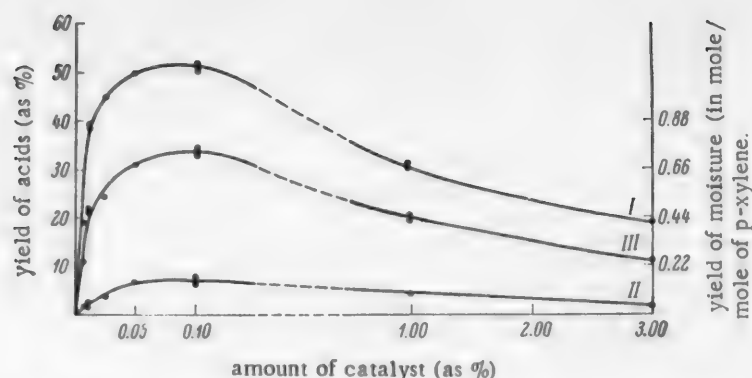
Fig. 3. Relationship between the yield of the main oxidation products
of p-xylene and the concentration of catalyst:
I) p- toluic acid;   II) terephthalic acid;   III) water.

Influence of the Amount of Catalyst on the Oxida-
tion of p-Xylene (Reaction Temperature 133-135°,
Duration of the Experiment 8 Hours)

Amount of cobalt acetate (as %)	Ratio between the yields of p-toluic and terephthalic acid	Maximum rate of liberation of moisture(in mole/mole of p-xylene per hour)	Induction period (in minutes)
0.001	—	—	more than 10 hrs
0.006	28.2	0.13	45
0.010	13.0	0.13	30
0.010	12.6	0.13	30
0.025	11.8	0.16	25
0.050	10.8	0.17	20
0.100	6.9	0.19	5
0.100	6.9	0.18	5
0.100	6.9	0.19	5
1.000	5.8	0.10	
1.000	6.2	0.11	} absent
3.000	17.2	0.13	

Under the given conditions, the minimum
permissible concentration of cobalt acetate is evi-
dently 0.005-0.006% (0.00004 g-at of cobalt per
mole of p-xylene) because with a lesser amount of
catalyst the reaction velocity and the yield of acids
were extremely low and the induction period in the
experiment with 0.001% catalyst lasted more than
10 hours. It must be noted, however, that even with
low amounts of catalyst the oxidation of p-xylene
can be intensified by the introduction of certain
readily oxidizable substances into the reaction mix-
ture. For example, in the experiments with 0.006%
cobalt acetate we succeeded in raising the total
yield of acids from 20 to 33% by the addition of 1%
p-toluic aldehyde, the reaction taking place in this
instance without an induction period and at a lower
temperature than usual (at 120°). The optimum
amount of cobalt acetate required for the oxidation
of p-xylene under the given conditions is, therefore,
between 0.05 and 0.20%. The existence of limiting
concentrations of catalyst can be explained from the
aspect of the theory of chain processes. With a small

amount of catalyst the number of chains it can produce is small and the rate of oxidation is low. With increasing
concentration of catalyst the number of chains increases but the probability of their rupture as a result of the
reaction of the catalyst with the free radicals of the oxidized substance also increases. In consequence, the
length of the chains decreases and the general reaction velocity therefore falls, passing through a maximum.

In all the above-described experiments the reaction ceased spontaneously as a result of the presence of
unreacted p-xylene in the reaction zone. Its amount depended on the concentration of the catalyst, the reaction
temperature, the rate of admission of oxygen and other factors. Even under optimum conditions, however, not
more than 62-65% of the initial substance taken was oxidized. Fig. 4 gives the results of certain experiments
which we carried out to find out the causes of this phenomenon. In one of these, the influence of repeated ad-
ditions of catalyst was investigated. The reaction was commenced with 0.01% cobalt acetate. The first additional
amount of catalyst (also 0.01%) was only introduced into the reaction mixture after the period of retardation of
oxidation had commenced. From Fig. 4 it is seen that the rate of liberation of moisture showed a certain in-
crease soon after the addition of the catalyst; after a certain period, however, it decreased again without reaching
the former value. A similar picture was also found with subsequent additions of the catalyst. In this experiment

the yield of p-toluic and terephthalic acids was 39.1 and 4.4% respectively, i.e. it was somewhat higher than in the case of 0.01% catalyst without further additions. At the same time, if these data are compared with the results of experiments in which this amount or even a somewhat lesser amount of catalyst was introduced all at once before the commencement of the experiment (for example, 0.025 or 0.05% cobalt acetate; Fig. 3), it may be noted that in the given instance the oxidation was much worse.
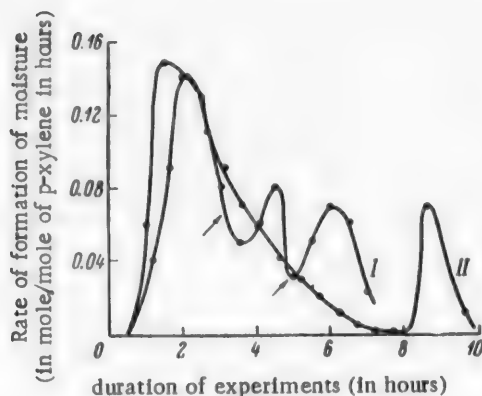

Fig. 4. The influence of repeated additions of catalyst on the process of the oxidation of p-xylene: I) with the addition of catalyst; II) with separation of the solid reaction products.
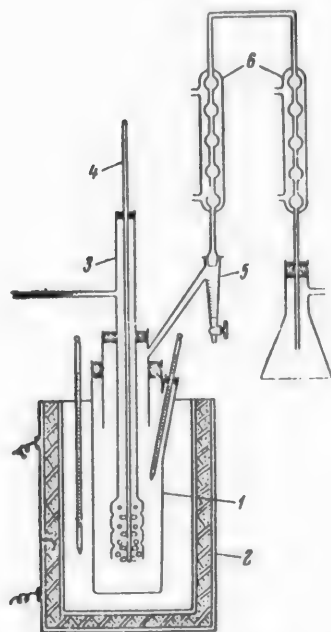

Fig. 5. Diagram of the apparatus for the oxidation of p-xylene. (Explanation in the text).

In another experiment, also carried out with 0.01% cobalt acetate, after the reaction had completely ceased and the reaction mixture had cooled, the latter was filtered through a No. 4 glass filter and the filtrate was oxidized again without the introduction of a further amount of catalyst. The reaction commenced after 40 minutes and continued for more than 2 hours. A further 11.1% of the acids was obtained, calculated on the p-xylene contained in the filtrate, or 4%, calculated on the initial product used.

A certain activation of the reaction as a result of the introduction of each fresh amount of cobalt acetate indicates that the catalyst had been used up during the process of oxidation of the p-xylene and makes it possible to assume that immediately before the introduction of the additional amount of catalyst there was a certain deficiency of the latter. This assumption is in agreement with literature data: during the oxidation of many hydrocarbons in the presence of salts of metals of variable valence it was noted that during the reaction process the catalyst undergoes irreversible conversions and in a number of instances is even precipitated [12-14].

However, the brief period of action of the fresh additions, the continued reduction in the total velocity of the process in spite of the fact that the total amount of cobalt acetate introduced in the form of additions is relatively great and, finally, the resutls of experiments with the filtering of the reaction products undoubtedly show that during the oxidation of p-xylene the catalyst is not completely used up and that a certain amount of it remains in an active state until the end of the reaction. The presence in the reaction zone of a large amount of p-toluic acid which reacts with the cobalt acetate with the formation of a salt of p-toluic acid evidently favors the conservation of the catalyst. The salt is readily soluble in p-xylene and also has the ability to catalyze the oxidation of aromatic hydrocarbons [15].

The results of the latter experiments show, therefore, that the autoretardation of the process of oxidation of p-xylene is not connected with the reduction in the concentration of the catalyst. It can also not be due to the presence of intermediate products of a phenolic character which, as was shown in the instance of p-toluic aldehyde [16], completely lose their inhibiting properties in the presence of a cobalt catalyst. The cause of the gradual retardation of the reaction velocity may be the gradual reduction of the concentration of p-xylene as a result of its dilution by the oxidation products; this must lead to a

progressive decrease in the length of the reaction chains. The final yield of the oxidation products also depends, without question. on the reactivity of the intermediate products, the concentration and activity of the free radicals which support the development of a chain reaction and many other factors [17].

The experimental data obtained in this work make it possible to express certain ideas regarding the mechanism of oxidative conversions of p-xylene itself, too. The main reaction products under the investigated conditions were p-toluic and terephthalic acids, which are evidently obtained via the intermediate formation of peroxide compounds and aldehydes according to the system:

$$R-CH_3 \rightarrow \underset{\underset{OOH}{|}}{R-CH_2} \rightarrow \underset{\underset{O}{\|}}{R-C-H} \rightarrow \underset{\underset{O}{\|}}{R-C-OOH} \rightarrow \underset{\underset{O}{\|}}{R-C-OH}$$

As was mentioned above, peroxides were actually present in the oxidation products but we did not succeed in establishing the presence of aromatic aldehydes (probably because of the ease with which they are oxidized).

The above-mentioned direction of the reaction was the principal one. Secondary reactions took place at the same time, leading to the formation of phenols. Their formation can be explained by the conversions of the intermediate peroxide compounds given below.

$$R-CH_2-OOH \rightarrow R-OH + CH_2O$$

$$R-C\underset{OOH}{\overset{O}{\diagup}} \rightarrow R-OH + CO_2$$
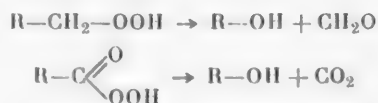
The importance of the secondary reactions was slight because the formaldehyde and carbon dioxide were present in very small amounts and the phenols were only detected qualitatively. Tarring-up and complete oxidation reactions hardly took place.

EXPERIMENTAL

The p-xylene used had an m.p of $13°$, a b.p. of $133°$ (700 mm), d_4^{20} 0.8621, n_D^{20} 1.4952. Cobalt acetate of C.P. grade was used as the catalyst.

The experiments were carried out in an apparatus represented diagrammatically in Fig. 5. The reaction vessel was a column of molybdenum glass (1), 27 mm in diameter and 400 mm high, heated by an electric oven (2). Oxygen was fed from a cylinder into the column via a bubbler(3), equipped with a mechanical stirrer (4). The column was connected to a graduated water trap (5) and condensers (6). In some experiments additional traps cooled by liquid air were installed after the condenser in order to collect the volatile reaction products and the vapors of unreacted p-xylene 53 g of p-xylene was generally introduced into the reaction vessel. In all experiments the oxygen was fed at a rate of 20-25 liters/hour, the feed commencing as soon as the given temperature in the reaction medium had been attained.

The rate of oxidation of the p-xylene was assessed from the amount of water collected in the trap. Samples were taken periodically from the reaction medium to determine the peroxide compounds by the iodometric method [18]. The acids were determined only after the completion of the experiment. To do this,the unreacted p-xylene was first removed from the reaction mass by steam distillation and the remaining mixture of p-toluic and terephthalic acids was then separated by extraction with benzene in a Soxhlet apparatus [19]. The acids were identified by their melting points and neutralization equivalents. In addition, the terephthalic acid was converted to the dimethyl ester. Phenols, present in the oxidation products as traces, were detected by their qualitative reaction with bromine water [20]. Formaldehyde and carbon dioxide were quantitatively determined in the reaction gases, the former as formaldimedone [21], the latter by absorption by caustic potash and baryta water.

SUMMARY

1. The reaction of the liquid-phase oxidation of p-xylene by molecular oxygen in the presence of cobalt

acetate was investigated. It was established that the main oxidation products of p-xylene under the investigated conditions are p-toluic and terephthalic acids.

2. It was shown that the catalyst plays the most important role in the initial period of the reaction. The scales and intensity of the initial stages of the process depend on the concentration of the catalyst and they de-termine the reaction velocity, its direction and extent.

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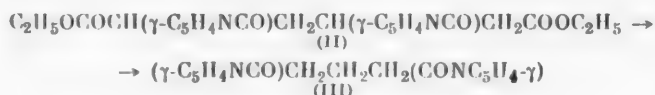# ETHYL ISONICOTINOYLACETATE AND ITS DERIVATIVES

II. CONDENSATION WITH ALDEHYDES AND AMINES

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In our previous paper [1] it was shown that ethyl isonicotinoylacetate (γ-C$_5$H$_4$NCO)CH$_2$COOC$_2$H$_5$ (I) is easily condensed, as a result of the activity of its keto group, with the formation of a number of heterocyclic compounds having a γ-pyridine radical. Both the ester (I) itself and the heterocyclic compounds obtained from it show chemical characteristics which differentiate them from ethyl benzoylacetate and the heterocyclics obtained from the latter. It was also of interest to investigate the degree of activity of the CH$_2$ group in the ester (I) and the readiness with which condensations based on the activity of the methylene group take place. It was also useful to determine the capacity of the carbethoxy group for condensation with aromatic o-diamines.

In the first place, the reaction with aldehydes was investigated. It was found that the ester (I) readily condenses with 0.5 mole of formaldehyde. Whereas Knoevenagel [2] required the participation of a condensing medium (diethylamine, etc.) for the condensation of ethyl benzoylacetate with formaldehyde, in our case the condensation took place smoothly without the addition of amines, probably as a result of the intramolecular influence of the basic properties of the pyridine ring. The condensation product, α, α'-diisonicotinoyl glutaric ester (II), was subjected to acid cleavage without being separated; this led to a good yield of 1,3-diisonicotinoyl-propane (III).

$$C_2H_5OCOCH(\gamma\text{-}C_5H_4NCO)CH_2CH(\gamma\text{-}C_5H_4NCO)CH_2COOC_2H_5 \rightarrow$$
$$(II)$$
$$\rightarrow (\gamma\text{-}C_5H_4NCO)CH_2CH_2CH_2(CONC_5H_4\text{-}\gamma)$$
$$(III)$$

Knoevenagel [3] and also Wislicenus and Carpenter [4] found that in an aqueous-alcoholic medium at 160°, 1,5-diketones and hydroxylamine medium give α, α'-disubstituted pyridines. The substance (III), was also subjected to this reaction, 38% being converted to α,α'-dipyridyl-(4')-pyridine (IV); the latter is a white crystalline substance capable of forming two series of salts, a readily soluble diacid salt and a less soluble monoacid salt. The indicated structure of the dipyridylpyridine obtained is confirmed by the infrared absorption spectrum * in the region from 2.5 to 14 μ, shown in Fig. 1. The substance was photographed in the solid crystalline state in the form of a suspension in vaseline oil.

(IV)
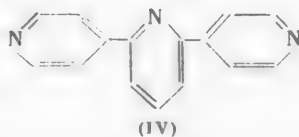
* The spectrum was determined and interpreted by Yu. N. Sheinker to whom we wish to express our sincere thanks.

Of the observed absorption bands note may be taken of the bands at 1581 and 1546 cm^{-1} which are characteristic, the first for (certain) γ-substituted pyridines, the second for α-substituted pyridines. These bands correspond to the asymmetric vibration of the pyridine rings. The band in the 996 cm^{-1} region, which is also observed with many other pyridine derivatives, evidently belongs to the symmetrical vibration of the pyridine ring.
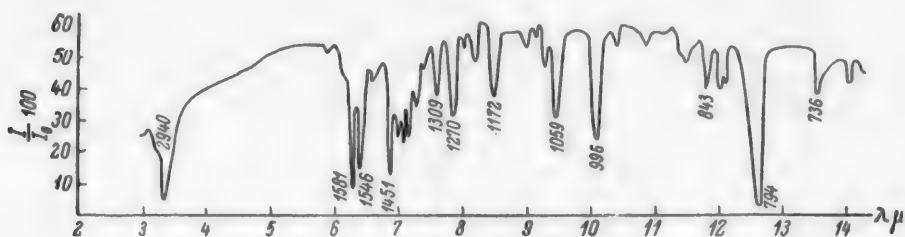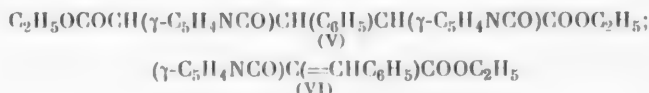

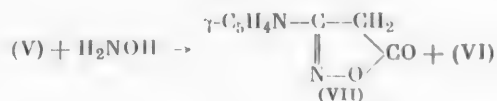Fig. 1. Infrared spectrum of α, α'-dipyridyl-(4')-pyridine.

As a result of the reduction of product (III) by the Meerwein-Ponndorf method with aluminum isopropylate [5], 1,5-di-(γ-pyridyl)-pentadiol, a dense, distillable, noncrystallizing mass was obtained.

The condensation of the ester (I) with m-nitrobenzaldehyde takes place normally, giving, after acid cleavage, 2-(m-nitrophenyl)-1,3-diisonicotinoylpropane, γ-C$_5$H$_4$NCOCH$_2$CH (m-C$_6$H$_4$NO$_2$)CH$_2$COC$_5$H$_4$N-γ, which with hydroxylamine gives a dioxime.

Condensation with unsubstituted benzaldehyde takes place more difficultly and in a more complex manner. For example, with equivalent quantities of ester (I) and benzaldehyde, two substances were obtained: the product of the reaction of 2 molecules of (I) with 1 molecule of benzaldehyde, with an m.p. of 102-103° and the product of their reaction in a ratio of 1:1, with an m p. of 110-112°. The first may be considered to have the structure of ethyl α,α'-diisonicotinoyl-β-phenylglutarate (V), and the second that of ethyl benzylidene-isonicotinoylacetate (VI).

$$C_2H_5OCOCH(\gamma\text{-}C_5H_4NCO)CH(C_6H_5)CH(\gamma\text{-}C_5H_4NCO)COOC_2H_5;$$
$$(V)$$
$$(\gamma\text{-}C_5H_4NCO)C(=CHC_6H_5)COOC_2H_5$$
$$(VI)$$

The structure of substance (V) was proven by the fact that it is soluble in solutions of alkalis and as a result of acid cleavage gives 1,3-diisonicotinoyl-2-phenylpropane with a good yield. When heated with dilute hydrochloric acid, compound (VI) splits off benzaldehyde and carboxyl, forming γ-acetopyridine. It is noteworthy that the double bond in compound (VI) does not have the characteristic properties of the unsaturated state: solutions of substance (VI) in chloroform do not decolorize bromine water and do not deoxidize permanganate. This phenomenon could be attributed to the characteristics of the -CO-C (=CHC$_6$H$_5$)-CO group. An analogous phenomenon is observed in the case of chalcone chains of similar structure when they add iodine [6]. Attempts to obtain oximes of substances (V) and (VI) led to major transformations. When substance (V) was heated with hydroxylamine in an aqueous-alcoholic medium, 3-(γ-pyridyl)-5-isoxazolone(VII)described by us previously [7], was obtained. The course of the reaction may be represented in the following manner:

$$(V) + H_2NOH \rightarrow \begin{matrix} \gamma\text{-}C_5H_4N\text{---}C\text{---}CH_2 \\ \| \quad \rangle CO + (VI) \\ N\text{---}O \\ (VII) \end{matrix}$$

The addition of compound (VI) with hydroxylamine gives the same pyridylisoxazolone and benzaldehyde. These conversions of compounds (III) and (IV) show that a weakening of the bond of the central (benzylidene)

169

carbon atom with the neighboring ones takes place in the groups

$$-CO \diagdown CH-CH(C_6H_5)-CH \diagup^{CO-}_{\diagdown CO-} \quad \text{and} \quad -COC(=CHC_6H_5)CO-$$
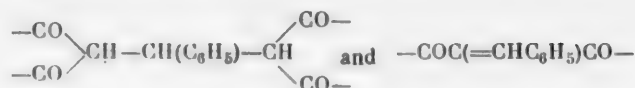
under the influence of the electrophylic attack of the hydroxylamine; as a result of this, hydrolysis of the bond and cleavage of the molecule take place, the monoxime probably being first formed and then immediately converted by closure into isoxazolone.

$$C_5H_4N-C-CH-CH-CH-COC_5H_4N$$
$$\underset{N}{\overset{||}{}} \quad \underset{CO}{} \quad \underset{C_6H_5}{} \quad \underset{COOC_2H_5}{}$$
$$O$$
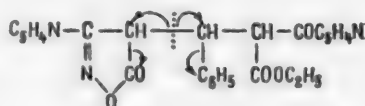
As a result of hydrolysis the formation of the substance

$$C_6H_5CH(OH)-CH-CO-C_5H_4N$$
$$\overset{|}{COOC_2H_5}$$,
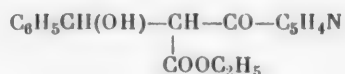
together with isoxazolone must take place but it is immediately dehydrated and forms ethylbenzylideneisonico-tinoylacetate(VI); closure of the oxazolone takes place and benzaldehyde is split off.

    The ester (I) also condenses with the acid chloride, though under somewhat different conditions, in a medium of acetic acid. As a result two substances are obtained: one, the predominating compound, with an m.p. of 139-141° and the other, formed in a lesser quantity and free from chlorine, with an m.p. of 307-310°. The substance with an m.p. of 139-141° is the normal product of the condensation of the ester (I) and chloral in a molar ratio of 1:1 and has the structure γ-$C_5H_4NCOCH(CHOHCCl_3)$-$COOC_2H_5$ or (2-trichloro-1-hydroxyethyl)-isonicotinoylacetic ester. This structure was proven by acid cleavage, which gave γ-pyridyl-(3-trichloro-2-hydroxypropyl)-ketone. The substance with an m.p. of 307-310° was not investigated in greater detail, however, because of the small amount available.

    When the ester (I) was condensed with salicylaldehyde the normal condensation products were not obtained and only a small amount of a yellow substance, probably isonicotinoylacetyl-isonicotinoylacetic acid (VIII),was obtained.

$$(\gamma\text{-}C_5H_4NCO)CH_2COCH(COC_5H_4N)COOH$$
$$(VIII)$$

    The condensation of the ester (I) with p-dimethylaminobenzaldehyde was also carried out in a molecular ratio of 2:1 in a medium of acetic acid.

    The carbethoxy group in the ester (I) determines a number of reactions characteristic of the latter, in-cluding the capacity to condense with o-phenylenediamine with the formation of benzimidazole derivatives. In the literature it is indicated [8] that in the condensation of acetoacetic ester with o-phenylenediamine,the addition of a small amount of an alkaline agent assists the formation of 2-acetonyl-benzimidazole. S. L. Davydova [9], however, describes the condensation of o-phenylenediamine with ethyl benzoylacetate by heating without an alkaline agent in xylene,with simultaneous distillation of alcohol and water, the yield being 81.8 %. The condensation which we carried out with the addition of a small amount of potash gave poor results. Better results are obtained if the condensation is carried out in a solution of xylene with distillation of the alcohol, water and, to a partial extent, the xylene.
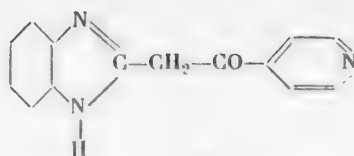
(IX)

(2-Benzimidazolyl)-methyl-(γ-pyridyl)-ketone (IX) was obtained as well-formed light-yellow prisms, only slightly soluble in organic solvents. The corresponding 5-methoxy derivative was also obtained. Taking into consideration the extremely high sensitivity of 3,4-diaminoanisole to atmospheric oxygen [10], m-nitro-p-anisidine was reduced in alcohol by hydrogen with PtO_2; after separation of the catalyst in an atmosphere of nitrogen, the ester (I) was then added to the filtrate, the solvent was distilled, xylene added and the condensation was carried out. The yield, calculated on the nitroanisidine, was only 20%. It is interesting to note that this ketone is also difficultly soluble in the usual organic solvents. Whereas (2-benzimidazolyl)-methyl-(γ-pyridyl)-ketone melts at 211-212°, the melting point of the methoxy derivative is 317°, i.e. the introduction of an electron-donating group intensifies the heteropolarity of the molecule. When boiled with 48% hydrobromic acid the methoxy derivative is converted smoothly to the hydroxy compound, which does not melt up to 370°; this is evidently due to the appearance of a hydrogen bond resulting from the hydroxyl function.

EXPERIMENTAL

The condensation of ethyl isonicotinoylacetate with formalin. 1,3-Diisonicotinoylpropane (III). 2 ml of 37% formalin was added with stirring over a period of 15 minutes to a solution of 9.7 g of the ester (I) in 20 ml of alcohol cooled to 10°. After being kept for 3 hours the homogeneous solution was heated on a boiling water bath for 4 hours with a reflux condenser. The alcohol was then distilled, 10 ml of 6 N hydrochloric acid was added to the residue and the solution was heated in an open flask on a boiling water bath for 3 hours. During this process the vigorous evolution of CO_2 bubbles was noted at the beginning. When the solution had cooled, it was neutralized with a 30% caustic soda solution. The precipitated oil crystallized rapidly in the form of light-brown granules. They were filtered, washed with water and recrystallized from 60% methanol. Large bright crystals of 1,3-diisonicotinoylpropane (III) were obtained. The m.p. was 92-93°. The yield was 5 g (78%).

Found %: N 11.1, 11.3. $C_{15}H_{14}O_2N_2$. Calculated %: N 11.0.

When substance (III) was dissolved in the theoretical amount of boiling 5% hydrochloric acid (calculated on the monohydrochloride) yellow prismatic crystals of the difficultly soluble monohydrochloride, with an m.p. of 254-256° (decomp.) were obtained.

Found %: C 12.3, 12.5. $C_{15}H_{14}O_2N_2 \cdot HCl$. Calculated %: C 12.2.

The dihydrochloride was readily soluble.

The dioxime of 1,3-diisonicotinoylpropane was obtained by heating 1 g of (III) with 0.6 g of hydroxylamine hydrochloride and 0.65 g of anhydrous sodium acetate in a medium of 5 ml alcohol + 3 ml H_2O. Well-formed, large, transparent, colorless prisms soon began to be precipitated. After they had been heated for 2 hours the crystals were filtered and washed with 50% alcohol. The yield was 1 g; it was in the form of well-formed prismatic needles with an m.p. of 197-198° (from 80% alcohol).

Found %: N 17.5, 15.5; H_2O 12.30. $C_{15}H_{16}O_2N_4 \cdot 2H_2O$. Calculated %: N 17.2; H_2O 12.2.

α,α'-Dipyridyl-(4')-pyridine (IV). 3 g of substance (III) and 2 g of hydroxylamine hydrochloride in 10 ml of 90% alcohol were heated in a sealed tube for 7 hours at 160-165°. When cooled, the contents of the tube were a dense mass of interlaced crystals. There was no pressure in the tube. The crystals of the hydrochloride were filtered and washed with alcohol. The m.p. was 280-285° (from hot water). The yield was 1.5 g (38%).

Found %: Cl' 10.5; H_2O 20.0. $C_{15}H_{11}N_3 \cdot HCl \cdot 4H_2O$. Calculated %: Cl' 10.4; H_2O 21.0.

α,α'-Dipyridyl-(4')-pyridine hydrochloride readily soluble in hot water, difficultly soluble in cold water, soluble in hot alcohol and almost insoluble in cold alcohol.

The straw-colored base of α, α'-dipyridyl-(4')-pyridine was precipitated from a solution of the hydrochloride with caustic soda. The m.p. was 144-146° (from ethylacetate).

Found %: N 17.7, 18.1; C 77.2, 77.3; H 4.8, 4.8. $C_{15}H_{11}N_3$. Calculated %: N 18.0; C 77.2; H 4.7.

The base was insoluble in water and aqueous alkalis, readily soluble in alcohol, chloroform, acetone and almost insoluble in ether. It gave two series of salts: in addition to the above-described hydrochloride, the very readily soluble dihydrochloride was obtained when the base was neutralized (to Congo red).

The picrate was obtained in an alcoholic medium. It was almost insoluble in water, alcohol and benzene; the m.p. was 252-254° (decomp.).

Found %: N 16.4, 16.6. $C_{15}H_{11}N_3 \cdot 2C_6H_2$ $(NO_2)_3OH \cdot 4H_2O$. Calculated %: N 16.5.

The reduction of 1,3-diisonicotinoylpropane (III). A solution of aluminum isopropylate was prepared in 1.5 hours from 1.25 g of aluminum chips in 25 ml of isopropyl alcohol with 2 drops of CCl_4 and a crystal of mercuric chloride. A solution of 2.54 g of substance (III) in 25 ml of isopropyl alcohol was added to it dropwise over a period of half an hour with gentle heating and stirring, after which the entire mass was boiled for 4 hours on a water bath. The major part of the isopropyl alcohol was then distilled and the residue was decomposed with a mixture of 5 ml of isopropyl alcohol with 5 ml of water; 10 ml of 40% caustic soda and 20 ml of H_2O were then added. The layers separated. The upper layer was separated and the lower was extracted twice with 15 ml of ether each time. The combined ethereal extracts together with the separated alcoholic solution were dried with anhydrous potash, the solvent was distilled off and the residue was distilled at a temperature of 242-245° (0.5 mm). The yield was 2.1 g (82%). It was a vitreous mass which did not crystallize.

Found %: N 10.4, 10.8. $C_{15}H_{18}O_2N_2$. Calculated %: N 10.8.

The condensation of ethyl isonicotinoylacetate with m-nitrobenzaldehyde. 1,3-Diisonicotinoyl-2-m-nitro-phenylpropane. 7.7 g of the ester (I), 3 g of m-nitrobenzaldehyde and 5 ml of alcohol were heated with stirring in a three-necked flask on a steam bath with gradual partial distillation of the alcohol over a period of 4 hours. The mass was neutralized (to Congo with 10% hydrochloric acid and extracted with ether. The aqueous solution was treated with 20% caustic soda until it gave a neutral reaction to litmus. The base precipitated; as a result it was a solidified granular mass. It was filtered, washed with water and dried. The weight was 9 g. Since it could not be recrystallized it was subjected to treatment with acid. 10 ml of concentrated hydrochloric acid and 6 ml of H_2O were taken for the 9 g of precipitate; the reaction mass was boiled on a grid with a reflux condenser for 3 hours. The solution was then neutralized with 10% caustic soda. A viscous colored oil, which did not crystallize, separated out. The aqueous solution was decanted and 5 ml of CH_3OH was added to the oil, after which it began to crystallize. The crystals were filtered, washed twice with 3 ml of CH_3OH each time and dried in a desiccator. 3.2 g of 1,3-diisonicotinoyl-2-m-nitrophenylpropane, with an m.p. of 151-152° (from CH_3OH), was obtained. The compound had the appearance of well-formed, straw-colored prismatic crystals.

Found %: N 11.3, 11.2. $C_{21}H_{17}O_4N_3$. Calculated %: N 11.2.

The dioxime of 1,3-diisonicotinoyl-2-m-nitrophenylpropane was obtained with hydroxylamine hydrochloride and anhydrous sodium acetate in a medium of alcohol. The m.p. was 258-260°. It was insoluble in alcohol, ether and acetone; it was very difficultly soluble in pyridine and glacial acetic acid.

Found %: N 17.2. $C_{21}H_{19}O_4N_5$. Calculated %: N 17.3.

The condensation of ethyl isonicotinoylacetate with benzaldehyde. A mixture of 9.7 g of ester (I), 5.8 g of benzaldehyde and 1 drop of pyridine was heated with stirring in a three-necked flask on a boiling water bath for 3 hours. The next day the partially crystallized reaction mass was treated with 5% hydrochloric acid until it gave an acid reaction to Congo. The solution obtained was extracted three times with ether. The aqueous solution was made alkaline with a 10% solution of caustic soda. The precipitated oil was separated from the aqueous solution and dissolved in hot 66-70% methanol. The next day the crystals (A) were separated and the filtrate was concentrated. Crystals (B) were again deposited from it overnight. Both substances were purified by several recrystallizations from 66-70% methanol and individually examined. Substance (A), which was less soluble in 70% methanol, had an m.p. of 93-95° and contained water of crystallization; after this had been removed the substance melted at 102-103°; substance (B) which was more soluble had an m.p. of 110-112°.

The investigation of substance (A) with an m.p. of 102-103° showed that it was the condensation product

of 2 moles of ethyl isonicotinoylacetate and 1 mole of benzaldehyde, i.e. ethyl benzylidenediisonicotinoylacetate (or α,α'-diisonicotinoyl-β-phenylglutaric acid (V)). It dissolved in solutions of alkalis, giving a faint yellow color.

Found % H_2O 4.5; N 5.7, 6.0; C 65.4, 65.5; H 5.2, 5.3. $C_{27}H_{26}O_6N_2 \cdot 1\frac{1}{2} H_2O$. Calculated % H_2O 4.8; N 5.6; C 65.0; H 5.2.

1 g of substance (A) was boiled with 5 ml of 20% hydrochloric acid on a grid for 3 hours. The solution darkened intensely. After it had been neutralized, a dark oil separated out; this crystallized out overnight to give a cream-colored mass. The liquid remaining was decanted and the residue was recrystallized from 3 ml of 60% methanol. 0.7 g of fine white crystals, with an m.p. of 102-103°, was obtained; on analysis this was found to be 2-phenyl-1,3-diisonicotinoylpropane.

Found %: H_2O 7.0; N 8.0, 8.2. $C_{21}H_{18}O_2N_2 \cdot H_2O$. Calculated %: H_2O 7.3; N 8.1.

The dehydrated 2-phenyl-1,3-diisonicotinoylpropane was recrystallized from a mixture of benzene and gasoline. The m.p. was 108-110°.

Substance (B) with an m.p. of 110-112° was found to be the condensation product of 1 mole of benzaldehyde and 1 mole of ethyl isonicotinoylacetate, i.e. ethyl benzylidene-isonicotinoylacetate (VI). It did not dissolve in solutions of alkalis.

Found % C 72.3, 72.0; H 5.6, 5.6. $C_{17}H_{15}O_3N$. Calculated % C 72.6; H 5.2.

Attempts to obtain the normal oximes of both compounds (A) and (B) led to major changes.

a) 0.3 g of (A), 0.09 g of hydroxylamine hydrochloride and 0.1 g of anhydrous sodium acetate were heated on a water bath with 5 ml of 50% alcohol for 2 hours. The solution darkened intensely and after it had cooled a yellow crystalline precipitate was deposited in the form of leaflets. It was separated, washed with 50% alcohol and dissolved in 5% caustic soda; the solution was then filtered and precipitated while hot, with acetic acid. Fine, well-formed yellow crystals were deposited. When they had been dried at 104-105° their m.p. was 194-195° (decomp.). A mixed melt with 3-(γ-pyridyl)-isoxazolone (VII) showed no depression of the melting point. A total of about 0.1 g was obtained.

b) 0.3 g of compound (B), 0.1 g of hydroxylamine hydrochloride, 0.12 g of CH_3COONa and 5 ml of 50% alcohol were taken. The mixture was heated on a boiling water bath with a reflux condenser. After 2 hours very few crystals had been precipitated; a further 0.1 g of hydroxylamine and 0.12 g of CH_3COONa were, there-fore, added and boiling was continued for another 4 hours. A total of 0.15 g of crystals was obtained and re-precipitated from alkali; the m.p. was 194-195°; the crystals were identical with substance (VII). The initial mother liquor had a strong odor of benzaldehyde.

The condensation of ethyl isonicotinoylacetate with salicylaldehyde. After an alcoholic solution of 9.8 g of ester (I) and 3.2 g of salicylaldehyde had been boiled on a water bath for 5 hours the alcohol was distilled off and the residue was neutralized with 5% hydrochloric acid. A small amount (1 g) of a yellow precipitate was deposited the amount increasing on the addition of ether. The precipitate was filtered and recrystallized from 5% alcohol. A considerable part of the salicylaldehyde used was recovered from the ethereal solution when the ether was distilled. The precipitate obtained was recrystallized from boiling alcohol; the m.p. was 261-262°.

Found %: N 9.1. $C_{16}H_{12}O_5N_2$. Calculated %: N 9.0.

The only product obtained from the condensation was, therefore, one which, from the analytical data, was probably isonicotinoylacetyl-isonicotinoylacetic acid (VIII).

The condensation of isonicotinoylacetate with chloral. 9.6 g of ester (I) and 8.3 g of chloral hydrate were taken . The mixture was heated on a steam bath with stirring. The mixture was all converted to a homo-geneous liquid. After 20-30 minutes the mass began to solidify. 10 ml of acetic acid was then added and heating was continued for a further 3 hours. The major part crystallized out overnight. The crystals were filtered, washed 3 times with 3 ml of 50% acetic acid each time and dried under vacuum over sulfuric acid and soda lime. 8 g of the substance was obtained and recrystallized from ethyl acetate. Part of the substance (2.5 g) was in-soluble and remained on the filter in the form of a fine crystalline powder. 2.9 g of crystals (needles and rhom-boids), with an m.p. of 137.5-142°, was obtained from the filtrate and the first mother liquor; these crystals were

again recrystallized from ethyl acetate. The crystals were filtered without being allowed to crystallize out completely; the m.p. was 139-141°. 0.3 g of a precipitate which was almost insoluble in the usual solvents and hardly contained chlorine was obtained from the mother liquor after concentration and treatment with methanol. After recrystallization from ethyl cellosolve it melted at 307-310°, almost completely subliming.

Analysis of the substance with an m.p. of 139-141°. Found %: Cl 31.4, 31.5. $C_{12}H_{12}O_4NCl_3$. Calculated %: Cl 31.2.

The substance obtained was, therefore, the addition product of chloral and ethyl isonicotinoylacetate: $C_5H_4NCOCH(CHOH-CCl_3)COOC_2H_5$.

To confirm the indicated structure.1 g of the substance with an m.p. of 139-141° was heated on a steam bath with 5 ml of 20% hydrochloric acid. A dense precipitate (acid chloride ?)was first formed but with further heating for 2 hours this slowly dissolved with the evolution of CO_2. The next day the solution was neutralized with sodium bicarbonate to a pH of 6. The precipitate deposited was filtered, washed with water, dried under vacuum and recrystallized from methanol. 0.3 g of γ-pyridyl-(3-trichloro-2-hydroxypropyl)-ketone, with an m.p. of 177-178°, was obtained. It was in the form of gray prisms, insoluble in cold water, chloroform and benzene, fairly soluble in methanol, ethanol and more soluble in hot solvents. When heated with aqueous solutions of alkali it gave a red-brown solution.

Found %: N 5.7, 5.8; Cl 39.5, 39.4. $C_9H_8O_2NCl_3$. Calculated %: N 5.3; Cl 39.6.

Analysis of the substance with an m.p. of 307-310°. Found %: N 11.2, 10.8. $C_{15}H_{12}O_2N_2$. Calculated %: N 11.1.

The condensation of ethyl isonicotinoylacetate with p-dimethylaminobenzaldehyde. A mixture of 9.5 g of substance (I), 3.7 g of p-dimethylaminobenzaldehyde and 5 ml of acetic acid was heated on a glycerine bath at 110-120° for 4 hours. 5 ml of water and 5 ml of methanol were then added to the reaction mass. The next day a crystalline precipitate was deposited from the dark-red solution; it was filtered, washed with 50% methanol and dried under vacuum over $CaCl_2$ + NaOH. The weight was 3.3 g. It consisted of yellow prisms of 2,5-diisonicotinoyl-3-(p-dimethylaminophenyl) glutaric ester. The m.p. was 137-138°. A further 1.3 g of a substance with an m.p. of 135-137° was obtained from the mother liquor after it had been concentrated; after recrystallization this substance melted at 136-137°. A picrate, with an m.p. of 128-129°, was obtained from the second mother liquor; this was identical with the picrate of γ-acetopyridine.

Found %: C 70.6, 70.5; H 6.2, 6.3; N 8.5, 8.1. $C_{19}H_{20}O_3N_2$. Calculated %: C 70.3; H 6.2; N 8.6.

The condensation of ethyl isonicotinoylacetate with o-phenylenediamine. (2-Benzimidazolyl-methyl)-γ-pyridyl-ketone. A mixture of 8.6 g of o-phenylenediamine, 15.4 g of ester (I) and 40 ml of xylene was heated gradually on a glycerine bath, first at 140-145° and then at 145-150° (temperature of the bath). At first a mixture of water, alcohol and xylene began to slowly distil. When half the xylene had distilled,the reaction mass suddenly crystallized. Heating was continued for a total of 1.5 hours. A 4 ml layer of alcohol and water separated out in the distillate. When it had cooled the precipitate was ground in a mortar with 10 ml of xylene, filtered, washed with alcohol, dried and recrystallized from ethyl Cellosolve. The yield of 2-benzimidazolyl-methyl--(γ-pyridyl) ketone was 15.5 g. A further 1 g of the substance was obtained from the mother liquor after concentration and dilution with alcohol. The yield was 16.5 g (91.5%). It consisted of well-formed, light-yellow prisms with an m.p. of 211-212°, very difficultly soluble in alcohol, ether, acetone and benzene; it was soluble in mineral acids.

Found %: N 17.9, 17.7. $C_{14}H_{11}ON_3$. Calculated %: N 17.7.

The acid chloride was obtained from 2.3 g of base in 15 ml of water by neutralization with 1.1 ml of hydrochloric acid (d 1.19), the mixture being heated. When the latter had cooled,light-yellow needles crystallized out; the m.p. was 230-235° in a sealed capillary (with darkening).

Found %: Cl 12.8, 13.0. $C_{14}H_{11}ON_3 \cdot$ HCl. Calculated %: Cl 12.9.

2-[4(5)-Methoxybenzimidazolyl]-methyl-(γ-pyridyl)-ketone. A solution of 9.5 g of m-nitro-p-anisidine in 60 ml of alcohol was hydrogenated over 0.15 g of PtO_2 at normal pressure. Hydrogen was absorbed intensely; after 2 hours the solution was almost decolorized and the absorption of hydrogen ceased. A total of 4220 ml of H_2

was absorbed (theoretical amount 4135 ml). The contents of the flask in which hydrogenation took place were transferred in a current of nitrogen to a funnel with a No. 1 glass filter containing a small filter paper; the solution of 3,4-diaminoanisole was filtered in a current of nitrogen and the residue of catalyst was washed with 5 ml of alcohol. The filtrate was transferred rapidly to a distillation flask containing a solution of 11.5 g of ethyl isonicotinoylacetate in 10 ml of alcohol; the alcohol was distilled off on a boiling water bath, 40 ml of anhydrous xylene was added to the residue and the mixture was heated on a glycerin bath at 140-150° (temperature of the bath). The water and alcohol (a total of 5 ml) were distilled in half an hour and 10 ml of xylene was then distilled in 1 hour. The next day the upper xylene layer was decanted from the solidified dense precipitate and the precipitate was dissolved with heating in 40 ml of methanol. When it had cooled a yellow precipitate was deposited (1.5 g). Concentrated hydrochloric acid was added to the mother liquor until an acid reaction to Congo was obtained and the mixture was left for 2 days. The precipitate deposited was filtered and dissolved in 30 ml of hot 5 % hydrochloric acid. A solution of 5 g of crystalline CH_3COONa in 5 ml of water was added to this solution. The fine, dark-red crystals of the monoacid chloride formed were filtered, washed with alcohol and a suspension of them in 30 ml of hot water was treated with a solution of ammonia; a yellow, fine-crystalline powder was deposited. Both the precipitate from methanol and that from the acid chloride were combined and recrystallized from pyridine. 3 g of the ketone, with an m.p. of 317-319° (in a sealed capillary) was obtained.

Found %: H_2O 6.3; N 15.18, 15.26; CH_3O 8.5. $C_{15}H_{13}O_2N_3 \cdot H_2O$. Calculated %: H_2O 6.3; N 14.83; CH_3O 10.8.

The diacid chloride was in the form of bright-yellow crystals with an m.p. of 275-277°.

Found %: Cl 19.1. $C_{15}H_{13}O_2N_3 \cdot 2HCl \cdot 2H_2O$. Calculated %: Cl 19.1.

2-[4(5)-Hydroxybenzimidazolyl]-methyl-(γ-pyridyl)-ketone. 0.5 g of 2-[4(5)-methoxybenzimidazolyl]-methyl-(γ-pyridyl)-ketone was dissolved in 10 ml of 48% hydrobromic acid and the solution was boiled with a reflux condenser for 5 hours. When the solution had cooled, well-formed, light-green crystals of the trihydrobromide were deposited (0.4 g). When heated to 370° it darkened but did not melt.

Found %; Br 47.2, 47.5; N 7.8, 8.1. $C_{14}H_{11}O_2N_3 \cdot 3HBr$. Calculated %: Br 48.2; N 8.4.

A further 0.15 g of hydrobromide was obtained from the mother liquor; after recrystallization from water this formed a brick-red crystalline powder of monohydrobromide.

Found %: Br 22.76, 23.19. $C_{14}H_{11}O_2N_3 \cdot HBr$. Calculated %: Br 23.85.

A solution of alkali was added to a solution of 0.1 g of the hydrobromide in water until the majority of the deposited precipitate had gone into solution. The solution was filtered and carefully acidified with acetic acid to a pH of 6. The yellow precipitate deposited was filtered, washed with water and dried. It darkened but did not melt up to a temperature of 370°.

Found %: N 15.15, 15.32. $C_{14}H_{11}O_2N_3 \cdot H_2O$. Calculated %: N 15.5.

SUMMARY

1. Ethyl isonicotinoylacetate has a very active methylene group capable of condensing with aldehydes (formalin, m-nitrobenzaldehyde, benzaldehyde, chloral), giving condensates in a ratio of 2:1 and 1:1.

2. Acid cleavage of the condensation products leads to the formation of pyridine derivatives of 1,5-diketones, hydroxyketones and γ-acetylpyridine.

3. Ethyl α, α'-diisonicotinoyl-β-phenylglutarate and ethyl benzylideneisonicotinoylacetate are unstable and when attacked by hydroxylamine in an aqueous-alcoholic medium split up giving 3-(γ-pyridyl)-(5)-isoxazolone and benzaldehyde.

4. When heated with hydroxylamine in a sealed tube at 160° diisonicotinoylpropane is converted to α, α'-dipyridyl-(4')-pyridine.

5. When heated with o-phenylenediamine and its methoxy derivatives, ethyl isonicotinoylacetate readily forms (2-benzimidazolyl)-methyl-(γ-pyridyl)-ketone and the corresponding methoxy compound.

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REACTION OF TERTIARY ALCOHOLS WITH UREA

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The reaction of tertiary alcohols with urea has been proposed for the synthesis of alkylureas [1], which after alkaline hydrolysis in ethylene glycol medium are easily converted to primary amines, with tertiary alkyl groups on the nitrogen [2], that are now not readily available. The reaction mentioned was recommended [1] for tert-butyl and tert-amyl alcohols and methyldiethylcarbinol.

The purpose of our investigation was to ascertain whether the method under consideration is general for tertiary alcohols. By the investigation of various carbinols we were able to ascertain (see Table 1) that only the simplest representative of the alcohols with one methyl group on the tertiary carbon reacts with urea. Alcohols with two methyl groups on the carbinol carbon react within considerably wider limits, but here also there are restrictions in connection with the nature of the third hydrocarbon group X. If X = phenyl or benzyl, then the reaction with urea practically does not go (alcohols 4 and 5). If X = a normal alkyl or has a branch at the end of the chain, then the tertiary alcohol reacts well with urea, although the yields of alkylurea decrease with the lengthening of the chain (alcohols 6-11). If X = a secondary radical, then the reaction goes poorly; thus, [dimethyl)(isopropyl)methyl]urea (from alcohol 12) was obtained in 1/5th the yield of [(dimethyl)(propyl)methyl]-urea (from alcohol 7), and the yield of [(dimethyl)(cyclohexyl)methyl]urea (from alcohol 13) proved to be insignificant. Alcohols in which the carbon connected with the carbonyl is quaternary (alcohols 14, 15) do not in general react in the manner specified (see Table 1).

TABLE 1

Yields of Alkylureas Obtained from Tertiary Alcohols

$$\begin{array}{c} R \\ R' \end{array} \!\!\! C-OH \longrightarrow \begin{array}{c} R \\ R' \end{array} \!\!\! C-NHCONH_2 \\ \begin{array}{c} R'' \end{array} \qquad \begin{array}{c} R'' \end{array}$$

Expt. No.	R	R'	R''	Yield (in %)
1	CH_3	C_2H_5	C_2H_5	34.7
2	CH_3	$n\text{-}C_3H_7$	$n\text{-}C_4H_9$	—
3	CH_3	$n\text{-}C_4H_9$	$n\text{-}C_4H_9$	—
4	CH_3	CH_3	C_6H_5	—
5	CH_3	CH_3	$C_6H_5CH_2$	—
6	CH_3	CH_3	C_2H_5	64.6 *
7	CH_3	CH_3	$n\text{-}C_3H_7$	54.1
8	CH_3	CH_3	$n\text{-}C_4H_9$	39.2 **
9	CH_3	CH_3	$iso\text{-}C_5H_{11}$	32.0
10	CH_3	CH_3	$n\text{-}C_6H_{13}$	31.6
11	CH_3	CH_3	$n\text{-}C_7H_{15}$	29.2
12	CH_3	CH_3	$iso\text{-}C_3H_7$	10.24
13	CH_3	CH_3	$CH_2\!\!\begin{array}{c}CH_2-CH_2 \\ CH_2-CH_2\end{array}\!\!CH$	0.54
14	CH_3	CH_3	$C(CH_3)_3$	—
15	CH_3	C_2H_5	$C(CH_3)_3$	—

*Prepared by the reaction of cyanamide and trimethylethylene with 60% yield and m.p. 156-158° [3].

**Prepared by the reaction of cyanamide and 2-methylhexene-2 with 12% yield and m.p. 102° [4].

TABLE 2

Preparation of Alkylureas

Expt. No.	Tertiary-alkylurea R-NHCONH$_2$ (R)	Reaction conditions: ratio of starting reagents (in moles)			Yield (in %)	Melting point	Solubility **						% Nitrogen	
		H$_2$SO$_4$	H$_2$NCONH$_2$	Tertiary alcohol			Alcohol	Acetone	Water	Dioxan	Ether	Benzene	Calculated	Found (average of two determinations)
1	CH$_3$-C(C$_2$H$_5$)(C$_2$H$_5$)(CH$_3$)	0.10:	0.05:	0.10	34.70	143.5—144°	++	+	-•••	-•••	-	-	19.44	19.47
2	C$_2$H$_5$-C(CH$_3$)(CH$_3$)	0.20:	0.10:	0.20	64.60	158—159	++	++	+	+	-	-	21.54	21.09
3	n-C$_3$H$_7$-C(CH$_3$)(CH$_3$)(CH$_3$)	0.10:	0.05:	0.10	54.10	123—124	++	++	-•••	+	+	+	19.44	19.45
4	n-C$_4$H$_9$-C(CH$_3$)(CH$_3$)(CH$_3$)	0.10:	0.05:	0.10	35.40	109—110	++	++	-•••	++	+	+	17.72	17.78
5	CH$_3$CH(CH$_3$)CH(CH$_3$)-C(CH$_3$)(CH$_3$)	0.15:	0.075:	0.15	32.01	108—109	++	++	-•••	++	+	-•••	16.28	16.67
6	n-C$_8$H$_{17}$-C(CH$_3$)(CH$_3$)	0.27:	0.130:	0.10	29.20	116—117	++	++	-•••	+	+	+	14.00	14.27
7	CH$_3$CH$_2$-CH(CH$_3$)-C(CH$_3$)(CH$_3$)	0.058:	0.029:	0.05	10.24	174.5—175	++	+	+	-•••	-	-	19.44	19.44
8	H$_3$C-CH$_2$... C(CH$_3$)(CH$_3$)	0.051:	0.025:	0.05	0.54	141—142	Not determined						15.22	14.99

*The reaction mixture was left overnight after stirring for 0.5 hour (experiments 1-3,8), 1 hour (experiments 4,5,7), or 2 hours (experiment 6). In experiment 7 and 8 allowing the reaction mixture to stand overnight resulted in obtaining a large amount of tarry product; therefore the reaction mixture was allowed to stand only for 0.5 hour after stirring in experiment 7 and for 1.5 hours in experiment 8. In experiment 8 the product was separated from the lower layer of the reaction mixture. The upper layer was a colorless liquid (4 g) that distilled at 152-168°. The boiling point of the dehydration product of dimethylcyclohexylcarbinol is 157-158° [8].

**In the "solubility" column (values given are in the cold) the following symbols are used: ++ soluble; + partly soluble; - insoluble.

***Dissolves in hot solvent.

The most important factor determining the capacity of tertiary alcohols to alkylate urea is apparently their greater or less tendency toward the competing dehydration reaction with the formation of unsaturated hydrocarbons (the reactions are carried out in concentrated sulfuric acid medium). As is known, the ability of alcohols to dehydrate increases with the extent of replacement of he hydrogens of the carbinol by less electrophilic alkyls and becomes greatest in the tertiary alcohols. It may be assumed that by replacing the more electrophilic radicals in the tertiary alcohols by less electrophilic ones — according to the series $H > CH_3 > C_2H_5 > > CH(CH_3)_2 > CH_2CH_2CH_3 > C(CH_3)_3$ [5] — the tendency to dehydration will also increase.

Actually, as can be seen from the data of Table 1, the yield of alkylureas decrease from alcohol 6 to alcohol 11 and reach zero for alcohols 14 and 15. When two alkyl radicals less electrophilic than methyl are present on the carbonyl group, the yields of alkylurea sharply decrease (alcohols 1-3). The low yield of alkylureas in the case of alcohols 12 and 13 can be explained by the known phenomenon of the easy dehydration of secondary alkylcarbinols in comparison with primary alkylcarbinols. Finally, alcohols 4 and 5 practically do not react with urea because their dehydration leads to the formation of energetically advantageous conjugated systems.

[(Dimethyl)(ethyl)-, [(dimethyl)(propyl)-, [(dimethyl)(butyl)-,[(dimethyl)(hexyl)-, and [(dimethyl)(heptyl) methyl]ureas were converted by us to the corresponding amines.

EXPERIMENTAL

(Carried out with the assistance of L. N. Chusova)

Preparation of tertiary-alkylureas. To a flask containing sulfuric acid (2 moles), and fitted with a stirrer, dropping funnel, and thermometer, was gradually added ground urea (1 mole) and then tertiary alcohol (2 moles) at such a rate as to hold the temperature at 20-25°. After this,the reaction mixture was stirred for some time and allowed to stand at room temperature. The contents of the flask either was a homogeneous, semitransparent, brown mass or formed two layers, the upper one of which — transparent and colorless in the main — consisted of unsaturated hydrocarbon and contained no alkylurea.

The whole reaction mass (or its lower layer) was poured into 2.5-3 volumes of water, and NaOH solution (20 %) was added until there was a weak alkaline reaction. The alkylurea that separated upon this treatment formed thin, colorless crystals, mixed with more or less oil. The crystals after filtration by suction and washing with water and ether were sufficiently pure to be used for preparation of the amines. The oil consisted of a mixture of the starting carbinol and unsaturated hydrocarbon.

Synthesis of [(dimethyl)(hexylmethyl]urea. 105 ml of H_2SO_4, 60 g of urea, and 288 g of dimethylhexylcarbinol under the conditions described above formed a reaction mixture that separated into two layers. From the upper layer (63.8 g) there was distilled off a product (33.5 g) that gave a positive qualitative reaction for an ethylenic bond and boiled at 141-146° • and 51-56° (18 mm).

[(Dimethyl)(hexyl)methyl]urea (50.6 g) was obtained from the lower layer of the reaction mixture together with a yellow oil that upon standing yielded crystals of alkylurea (8.2 g) with m.p. 109-113°. Total yield 31.6 %. The product dissolved very readily in alcohol and acetone, less readily in dioxan, poorly in ether and benzene, and very poorly in water. The pure compound melted at 120-121°.

Found %: N 15.14. $C_{10}H_{20}O_2$. Calculated %: N 15.20.

The yellow oil (103.1 g) upon vacuum fractional distillation yielded a mixture (30 g) of alkene and the starting alcohol (with a predominance of the former with b.p. 55-76° at 18 mm), and a mixture (43.6 g) of the same products with a predominance of the latter with b.p. 73-86° at 12 mm. The residue (28 g) was a thick, tarry mass.

The experiments on the preparation of the other alkylureas are presented in Table 2.

Reaction of methyldipropylcarbinol with urea and sulfuric acid. • When 13 g of methyldipropylcarbinol was added to a mixture of 5.5 ml of sulfuric acid and 3 g of urea, the evolution of heat was scarcely noticed. After the reaction mixture had been stirred for 2 hours, poured into water, and neutralized, 8 g of a colorless oil separated that distilled at 116-120° almost without residue (b.p. of 4-methylheptene-3 is 115-120° [9]).

Preparation of amines. In a round-bottomed flask fitted with a reflux condenser was placed a solution of sodium hydroxide (0.15 mole) in water (7.5 ml), tertiary alkylurea (0.06 mole), and ethylene glycol (22.5 ml); the mixture was boiled for 4 hours. On cooling, the amine obtained and the water were distilled off from the reaction vessel. The aqueous layer was saturated with alkali, the amine was separated and dried with solid NaOH, and then distilled at ordinary pressure. The results are given in Table 3.

TABLE 3

Preparation of Amines from Alkylureas

Amine	Boiling point	Yield (in %)
$C_2H_5C(CH_3)_2NH_2$	$74 - 79^\circ$	82.8
n -$C_3H_7C(CH_3)_2NH_2$	$101 - 103$	62.5
n -$C_4H_9C(CH_3)_2NH_2$	$124 - 127$	63.2
n -$C_6H_{13}C(CH_3)_2NH_2$	$170 - 174$	63.4
n -$C_7H_{15}C(CH_3)_2NH_2$	$188 - 192$	61.5

SUMMARY

1. A number of mono-tert-alkylureas have been synthesized. In this process, the capacity of tertiary alcohols of different structures to alkyiate urea has been studied, as a result of which the limits of usefulness of this reaction have been ascertained to a great extent.

2. The following new compounds have been described: [(dimethyl)(n-propyl)-, [(dimethyl)(isopropyl)-, [(dimethyl)(isoamyl)-, [(dimethyl)-(n-hexyl)-, [(dimethyl)(n-heptyl)-, [(dimethyl)-(cyclohexyl)-, and [(methyl) (diethyl)methyl]ureas, and [(dimethyl)(n-heptyl)methyl]amine.

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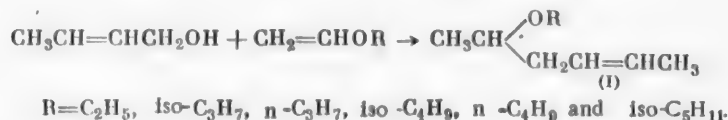*B.p. of 2-methyloctene-1 is 141.5-143° [6]; of dimethylhexylcarbinol,81° (13 mm) [7].

**Similar results were obtained in experiments with methyldibutyl-, dimethylphenyl-, dimethylbenzyl-, dimethyl-tert-butyl-, and methylethyl-tert-butylcarbinols.

SYNTHESIS OF ETHYL, ISOPROPYL, n-PROPYL, ISOBUTYL, n-BUTYL AND ISOAMYL CROTYL ACETALS

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The acetals of unsaturated ethylenic aclohols (I) have been little studied. However, they can be used for various chemical conversions. The present investigation had as its objective the synthesis of acetals from crotyl alcohol and vinyl alkyl ethers according to the following scheme

$$CH_3CH=CHCH_2OH + CH_2=CHOR \rightarrow CH_3CH \underset{CH_2CH=CHCH_3}{\overset{OR}{<}}$$
$$(I)$$

$$R=C_2H_5, \text{ iso-}C_3H_7, \text{ n-}C_3H_7, \text{ iso-}C_4H_9, \text{ n-}C_4H_9 \text{ and iso-}C_5H_{11}.$$

The addition of crotyl alcohol to the vinyl alkyl ethers proceeds with the evolution of heat. 30% hydrochloric acid was used as the catalyst. The ethyl, isopropyl, n-propyl, isobutyl, n-butyl, and isoamyl crotyl acetals prepared were colorless, mobile liquids with a pleasant odor. Quantitative hydrogenation of the acetals [1] confirmed the presence in them of one double bond. The hydrogenation products isolated had constants close to those described in the literature [2]. The purity of the acetals was determined by preparation of the oximes [3].

EXPERIMENTAL

The starting vinyl ethers were prepared by vinylation of the corresponding alcohols by the method of Favorskii and Shostakovskii [4]. Crotyl alcohol (b.p. 120-122°, n_D^{20} 1.4280) was prepared by hydrolyzing, with a 10% sodium carbonate solution, the bromide obtained by the hydrohalogenation of divinyl in glacial acetic acid [7].

Synthesis of ethyl crotyl acetal   In a three-necked flask fitted with a thermometer, a stirrer, and a reflux condenser with a calcium chloride tube were placed 10 g of crotyl alcohol and 20 g of vinyl ethyl ether (b.p. 35.5°, d_4^{20} 0.7527, n_D^{20} 1.3771). The vinyl ethyl ether was used in excess so that the unsaturated alcohol would react completely. 0.010 ml of 30% hydrochloric acid was added, with stirring. The temperature rose spontaneously to 40-65°. The mixture was allowed to stand overnight. To neutralize the hydrochloric acid, the reaction mixture was stirred with potassium carbonate for 2-3 hours, then filtered, and distilled twice in vacuo. 14 g (70%) of ethyl crotyl acetal was obtained.

B.p. 46.5-48.5° (13-14 mm), d_4^{20} 0.8505, n_D^{20} 1.4148, MR_D 42.44; calc. 41.96.

Found %: C 66.57, 67.05; H 10.97, 11.13. M 146.3. $C_8H_{16}O_2$. Calculated %: C 66.62; H 11.18. M 144.2.

The acetaldehyde content was determined in the acetals by preparation of the oximes.

Found %: acetaldehyde 98.4, 100.6.

Synthesis of isopropyl crotyl acetal. The reaction was carried out as in the preceding experiment. By the reaction of 10 g of crotyl alcohol and 18 g of vinyl isopropyl ether (b.p. 56-57°, n_D^{20} 1.3863), 17.8 g (80%) of isopropyl crotyl acetal was obtained.

B.p. 69-71° (23 mm), d_4^{20} 0.8461, n_D^{20} 1.4156, MR_D 46.89; calc. 46.58.

Found % C 68.64, 68.58; H 11.38, 11.20. M 158.3 $C_9H_{18}O_2$. Calculated % C 68.31; H 11.46. M 158.2.

Found % acetaldehyde 99.4, 99.8.

Synthesis of n-propyl crotyl acetal. By the reaction of 10 g of crotyl alcohol and 18 g of vinyl n-propyl ether (b.p. 65-66°, n_D^{20} 1.3923), 16.3 g (74.1%) of n-propyl crotyl acetal was obtained.

B.p. 78-80° (23-24 mm), d_4^{20} 0.8516, n_D^{20} 1.4190, MR_D 46.92; calc. 46.58.

Found % C 68.53, 68.51; H 11.22, 11.32. M 157.2. $C_9H_{18}O_2$. Calculated % C 68.31; H 11.46. M 158.2.

Found % acetaldehyde 99.0, 98.9

Synthesis of isobutyl crotyl acetal By the reaction of 8.4 g of crotyl alcohol and 12 g of vinyl isobutyl ether (b.p. 81-82°, n_D^{20} 1.3980), 13 g (65%) of isobutyl crotyl acetal was obtained.

B.p. 53-56° (7 mm), d_4^{20} 0.8462, n_D^{20} 1.4207, MR_D 51.58; calc. 51.20.

Found % C 69.82, 69.53; H 11.51, 11.61. M 167.0. $C_{10}H_{20}O_2$. Calculated % C 69.72; H 11.76. M 172.2.

Found % acetaldehyde 99.9, 99.2.

Synthesis of n-butyl crotyl acetal. By the reaction of 7 g of crotyl alcohol and 20 g of vinyl n-butyl ether (b.p. 93.5-94.5°, d_4^{20} 0.7790, n_D^{20} 1.4023), 11 g (71.7%) of n-butyl crotyl acetal was obtained.

B.p. 69-71° (9-10 mm), d_4^{20} 0.8493, n_D^{20} 1.4226, MR_D 51.60; calc. 51.20.

Found % C 69.73, 70.09; H 11.46, 11.71. M 170.4. $C_{10}H_{20}O_2$. Calculated %: C 69.72; H 11.76. M 172.2.

Found % acetaldehyde 101.8, 101.2.

Synthesis of isoamyl crotyl acetal. By the reaction of 8.5 g of crotyl alcohol and 13.5 g of vinyl isoamyl ether (b.p. 109-111°, n_D^{20} 1.4071), 13.2 g (60%) of isoamyl crotyl acetal was obtained.

B.p. 65-66° (5-6 mm), d_4^{20} 0.8500, n_D^{20} 1.4250, MR_D 56.03; calc. 55.82.

Found %: C 71.01, 71.22; H 11.75, 11.68. M 182.9. $C_{11}H_{22}O_2$. Calculated % C 70.91; H 11.90. M 186.2.

Found % acetaldehyde 100.4, 100.4.

Hydrogenation of the acetals was carried out on a Raney nickel catalyst with vigorous shaking. After the absorption of hydrogen ceased, the product was washed with ether, filtered off from the nickel, and fractionated in vacuo.

a) When 2.3 g of ethyl crotyl acetal was hydrogenated, 328 ml of hydrogen (108%) was absorbed. 1.1 g (41%) of ethyl butyl acetal was obtained.

B.p. 45° (14-15 mm), d_4^{20} 0.8266, n_D^{20} 1.3980, MR_D 42.56; calc. 42.43.

According to [2,5]: b.p. 145-147°, d_4^{20} 0.8312, n_D^{20} 1.3991.

b) When 2.8 g of isopropyl crotyl acetal was hydrogenated, 406 ml of hydrogen (103%) was absorbed in 2 hours. 2.2 g of isopropyl butyl acetal (79.6%) was obtained.

B.p. 64-65° (23 mm), d_4^{20} 0.8212, n_D^{20} 1.4000, MR_D 47.30; calc. 47.05.

According to [2]: b.p. 156-157°, d_4^{20} 0.8239, n_D^{20} 1.39985.

c) When 3 g of n-propyl crotyl acetal was hydrogenated, 438 ml of hydrogen (103%) was absorbed in 3 hours. 2.3 g (77%) of n-propyl butyl acetal was obtained.

B.p. 58-59° (13 mm), 164-166° d_4^{20} 0.8283, n_D^{20} 1.4033, MR_D 47.24; calc. 47.05.

According to [2]: b.p. 160-165°, d_4^{20} 0.8292, n_D^{20} 1.4038,

d) When 2.5 g of isobutyl crotyl acetal was hydrogenated, 350 ml of hydrogen (105%) was absorbed in 3 hours. 1.9 g (74.9%) of isobutyl butyl acetal was obtained.

B.p. 52-54° (6-7 mm), d_4^{20} 0.8250, n_D^{20} 1.4061, MR_D 51.89; calc. 51.66.

According to [2]: b.p. 74-76° (18 mm), d_4^{20} 0.8235, n_D^{20} 1.4062.

e) When 2.6 g of n-butyl crotyl acetal was hydrogenated, 371 ml of hydrogen (107%) was absorbed. 0.72 g (31%) of dibutyl acetal was obtained.

B.p. 60-62° (8-9 mm), d_4^{20} 0.8298, n_D^{20} 1.4090, MR_D 51.96; calc. 51.67.

According to [6] : b.p. 185-186°, d_4^{20} 0.8351, n_D^{20} 1.4087.

f) When 3.2 g of isoamyl crotyl acetal was hydrogenated, 415 ml of hydrogen (106%) was absorbed in 3 hours. 2.4 g (73.2%) of isoamyl butyl acetal was obtained.

B.p. 62-63° (5-6 mm), d_4^{20} 0.8295, n_D^{20} 1.4120, MR_D 56.48; calc. 56.28.

According to [2]: d_4^{20} 0.8313, n_D^{20} 1.4120.

SUMMARY

Ethyl, isopropyl, n-propyl, isobutyl, n-butyl, and isoamyl crotyl acetals have been prepared and characterized.

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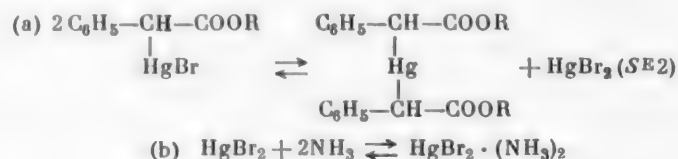[7] A. A. Petrov, J. Gen. Chem., 11, 9 (1941).

*Original Russian pagination. See C. B. translation.

STEREOCHEMISTRY OF THE REACTION OF 3-BROMOMERCURI-L-CAMPHOR AND 3-BROMOMERCURI-D-CAMPHOR WITH SODIUM THIOSULFATE

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It has been established by A. N. Nesmeyanov, S. A. Poddubnaya, and one of us [1] that in the symmetrization of the diastereomeric L-menthyl esters of α-bromomercuriphenylacetic acid with ammonia in chloroform, which is an electrophilic substitution on a saturated carbon atom, the stereochemical configuration is preserved.

Study of the kinetics of this reaction has shown [2] that it is a two-stage process.

(a) $2\,C_6H_5-\underset{\underset{\text{HgBr}}{|}}{CH}-COOR \;\rightleftarrows\; \underset{\underset{C_6H_5-CH-COOR}{|}}{\overset{C_6H_5-CH-COOR}{|}}Hg \;+\; HgBr_2\,(S_E2)$

(b) $HgBr_2 + 2NH_3 \rightleftarrows HgBr_2 \cdot (NH_3)_2$

The first stage (a) is a bimolecular, electrophilic substitution reaction.

In the present communication the results of further investigation of the stereochemistry of the symmetrization reaction, as represented in the example of organomercury derivatives of camphor, are reported.

A mixture of the diastereomers of 3-bromomercuri-L-camphor and a mixture of the diastereomers of 3-bromomercuri-L-camphor and a mixture of the diastereomers of 3-mercuri-D-camphor were prepared by mercurating L- and D-camphor, respectively, with K_2HgI_4 [3]. From the first mixture we separated by fractional crystallization from acetone the two diastereomers of 3-bromomercuri-L-camphor, which differed from each other in the configuration on the α-carbon atom. (I) (m.p. 222-223, $[\alpha]_D^{18}-30.7\pm1.2$); (II) (m.p. 216-218, $[\alpha]_D^{18}-126\pm1.9$). From the second mixture we separated the diastereomers of 3-bromomercuri-D-camphor: (III) (m.p. 222-223 $[\alpha]_D^{18}+28.7\pm1.2$); (IV) (m.p. 216-218, $[\alpha]_D^{18}+126.3\pm1.7$). The diastereomers (I) and (III) were more stable than diastereomers (II) and (IV). Thus, for example, diastereomer (I) was not converted into diastereomer (II) to an appreciable extent even in boiling xylene. Diastereomer (II), however, was partially converted into diastereomer (I) in boiling acetone.

Only sodium thiosulfate and hydrazine hydrate proved to be suitable as symmetrizing agents for all of these organomercury compounds, since the other usual symmetrizing agents either did not react at all with these organomercury compounds (ammonia), or brought about the rupture of all the carbon mercury bonds (KI, KOH, KCNS, Na_2S, Na_2SnO_2).

The symmetrization of the diastereomer (I) of 3-bromomercuri-L-camphor ($[\alpha]_D^{18}-29.5\pm1.1°$) with sodium thiosulfate (30% excess) was carried out in a mixture of water and benzene • with vigorous stirring for 2 hours in the cold. After the reaction was ended, the benzene layer was separated, the benzene was evaporated


• The mercurybiscamphor formed gradually is decomposed by the sodium thiosulfate. When a heterophase system (benzene-water) is used, the symmetrical organomercury compound formed (considerably more soluble in benzene than the unsymmetrical compound) goes into the benzene layer and thus is preserved from decomposition.

in the cold, the solid residue was washed with water, and then with ether (to remove camphor). • After recrystallization from aqueous dioxan the mercuribiscamphor melted at 229-230° (decomp.) and had $[\alpha]_D^{18} - 165.9° \pm \pm 1.1°$. The material obtained was almost exclusively the one isomer. This follows from the fact that when unrecrystallized mercuribis- L-camphor is reacted with an equimolecular amount of an alcoholic solution of hydrogen bromide, almost pure diastereomer (I) of 3-bromomercuri-L-camphor, after washing with water and ether,($[\alpha]_D^{18} - 38.8° \pm 1.8°$ • •)is formed.

Under identical conditions, the symmetrization of diastereomer (III) of 3-bromomercuri-D-camphor was carried out. When the mercuribis -D-camphor obtained unrecrystallized) was reacted with an equivalent amount of alcoholic solution of hydrogen bromide, almost pure diastereomer (III) was formed ($[\alpha]_D^{18} + 37.2° \pm \pm 2.7°$ after washing with water and ether).

It should be noted that the configuration on the α-carbon atoms of the mercuribiscamphor is more easily changed than in the bromomercury compounds. Thus, for example, 2 hours'heating in aqueous dioxan of the mercuribiscamphor obtained by the symmetrization of pure diastereomer (I) changed the mercuribiscamphor so much that upon treatment with hydrogen bromide a mixture of diastereomers of 3-bromomercuri-L-camphor was obtained that consisted of approximately 75% diastereomer (I) and 25% diastereomer (II). When the mercuri-biscamphor was recrystallized from aqueous dioxan, the angle of rotation of the compound also was not preserved. stereomer (II). When the mercuri-bis-camphor was recrystallized from aqueous dioxan, the angle of rotation of

The transformations of the organomercury derivatives of L- and D- camphor studied by us can be summarized by the following diagram.
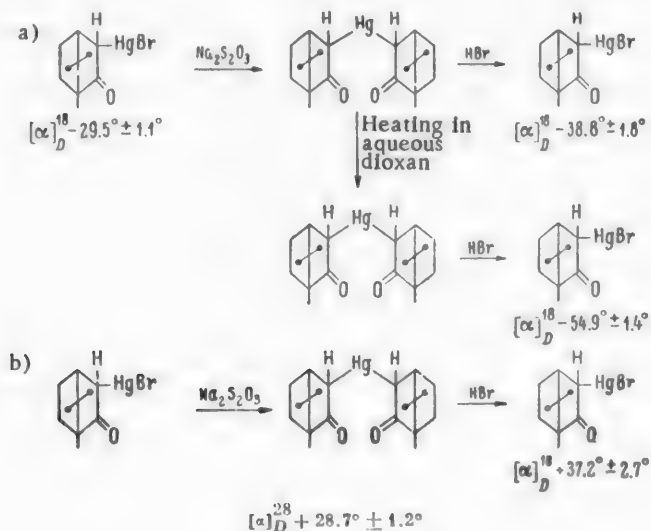

From the results stated above it follows that the symmetrization of organomercury salts by sodium thiosulfate, which is an electrophilic substitution reaction on a saturated carbon atom, takes place without change in the configuration.

• The mecuri-bis-camphor is very poorly soluble in ether.
• •Even if the excessive angle of rotation of the unrecrystallized material (-38.8°± 1.8° instead of -29.5° ± 1.1°) was entirely due to contamination with the second diastereomer of 3-bromomercuri-L-camphor with $[\alpha]_D^{18}$ -126°± 1.9°),still the amount of this isomer was less than 10%. The presence of this contaminant may be due to the fact that parallel with the symmetrization reaction in the weakly alkaline medium of the aqueous sodium thiosulfate solution there occurs a much slower racemization of the configuration of the α-carbon atom of the starting compound (diastereomer I or III) and of the final organomercury compound.
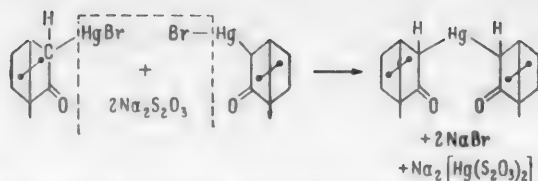
The question of whether the sodium thiosulfate reacts directly with the molecules of the organomercury salts or if the reaction proceeds in two stages

$$2\ R-HgBr \rightleftarrows R-Hg-R + HgBr_2$$
$$HgBr_2 + 2Na_2S_2O_3 \rightleftarrows Na_2[Hg(S_2O_3)_2] + 2NaBr,$$
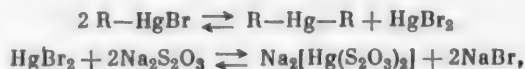
is still open.

EXPERIMENTAL

1. Separation of the diastereomers of 3-bromomercuri-L-camphor and 3-bromomercuri-D-camphor. 20 g of a mixture of the diastereomers of 3-bromomercuri-L-camphor ($[\alpha]_D^{18} - 74.4° \pm 1.8°$) was dissolved by boiling in 600 ml of 60% aqueous dioxan; the hot solution was filtered. When the solution cooled, 8 g of precipitate separated with $[\alpha]_D^{18} - 40.8 \pm 1.2°$ (c 2.13*, l 1.9, $\alpha - 1.65° \pm 0.05°$). After a second recrystallization from an appropriate amount of 60% aqueous dioxan the material had $[\alpha]_D^{18} - 36.4° \pm 1.1°$ (c 2.38, l 1.9, $\alpha - 1.65° \pm \pm 0.05°$). After a third recrystallization $[\alpha]_D^{18} - 36.4° \pm 1.1°$ (c 1.04 l 1.9, $\alpha - 0.8° \pm 0.05°$). After four recrystallizations, pure diastereomer (I) was isolated with $[\alpha]_D^{18} - 30.7° \pm 1.2°$ (c 2.14, l 1.9, $\alpha - 1.25° \pm 0.05°$) and m.p. 220-222°. Upon further recrystallization the specific rotation did not change.

Found %: C 27.39, 27.34; H 3.62, 3.57. $C_{10}H_{15}OHgBr$. Calculated % C 27.82; H 3.52.

The second diastereomer was isolated from the filtrate. The filtrate after the first recrystallization of the mixture of diastereomers was evaporated to half its volume. A precipitate separated out with $[\alpha]_D^{18} - 88.2° \pm \pm 1.2°$ (c 2.24, l 1.19, $\alpha - 3.75° \pm 0.05°$). After the separation of the precipitate, the filtrate was evaporated again to half its volume. A precipitate separated with $[\alpha]_D^{18} - 121.8° \pm 1.1°$ (c 2.44, l 1.9, $\alpha - 5.65° \pm 0.05°$). After a third evaporation of the filtrate to half its volume $[\alpha]_D^{18} - 122.3° \pm 1.1°$ (c 1.21, l 1.9, $\alpha - 2.85° \pm 0.05°$). After a fourth evaporation of the filtrate to half its volume, pure diastereomer (II) of 3-bromomercuri-L-camphor was isolated with $[\alpha]_D^{18} - 126.9° \pm 1.9°$ (c 1.38, l 1.9, $\alpha - 3.30° \pm 0.05°$) and m.p. 216-218°. Upon further fractional evaporation of the solvent, the specific rotation of the precipitates did not change.

Found %: C 27.91, 27.93; H 3.60, 3.54. $C_{10}H_{15}OHgBr$. Calculated % C 27.82; H 3.52.

The separation of the mixture of diastereomers of 3-bromomercuri-D-camphor was carried out in exactly the same way. Diastereomer (III) was isolated with $[\alpha]_D^{18} + 28.7° \pm 1.2°$ (c 2.29, l 1.9, $\alpha + 1.25° \pm 0.05°$) and m.p. 222-223°.

Found % C 27.76, 27.45; H 3.54, 3.64. $C_{10}H_{15}OHgBr$. Calculated % C 27.82; H 3.52.

Diastereomer (IV) was obtained with $[\alpha]_D^{18} + 126.3° \pm 1.7°$ (c 1.52, l 1.9, $\alpha + 3.65° \pm 0.05°$) and m.p. 216-218°.

Found % C 28.11, 28.18; H 3.61, 3.65. $C_{10}H_{15}OHgBr$. Calculated % C 27.82; H 3.52.

2. Heating 3-bromomercuri-L-camphor in xylene. A solution of 1.25 g of 3-bromomercuri-L-camphor ($[\alpha]_D^{18} - 48.2° \pm 2.7°$) in 100 ml of xylene was boiled for 6 hours. The solvent was distilled off in vacuo. The specific rotation of the compound was practically unchanged $[\alpha]_D^{18} - 45.9° \pm 2.2°$ (c 2.42, l 1.9, $\alpha - 2.1° \pm \pm 0.05°$).

3. Recrystallization of diastereomer (II) of 3-bromomercuri-L-camphor from acetone. 0.8 g of 3-bromomercuri-L-camphor ($[\alpha]_D^{18} - 126.0° \pm 1.9°$) was dissolved by boiling in 20 ml of acetone. The solution was cooled, and the precipitate that separated out was filtered off. $[\alpha]_D^{18} - 112.6° \pm 1.0°$ (c 2.64, l 1.9, $\alpha - 5.65° \pm \pm 0.05°$). The filtrate was evaporated to dryness. $[\alpha]_D^{18} - 113.2° \pm 2.0°$ (c 0.86, l 1.9, $\alpha - 1.85 \pm 0.05°$).

*The concentration c is everywhere expressed in grams of compound per 100 ml of solvent.

4. Symmetrization of mixture of diastereomers of 3-bromomercuri-L-camphor and mixture of diastereo-mers of 3-bromomercuri-D-camphor with sodium thiosulfate. 50 ml of water was poured over 10 g of 3-bromo-mercuri-L-camphor and then 50 ml of benzene was added. To this mixture was added dropwise, over a period of 30 minutes with vigorous stirring in the cold,an aqueous solution of 6 5 g of sodium thiosulfate, (12% excess). The 3-bromomercuri-L-camphor gradually dissolved. After an additional $1\frac{1}{2}$ hours' stirring, the benzene layer was separated and the benzene was evaporated to dryness. The weight of 3,3'-mercuribis-L-camphor, which was a white crystalline powder, was 4.6 g (79%). After two recrystallizations from aqueous dioxan the m.p. was 200-210° (decomp.). •

Found %: C 47.63, 47.79; H 6.32, 6.10. ($C_{10}H_{15}O)_2$Hg. Calculated %: C 47.79, H 6.01.

The symmetrization of the mixture of diastereomers of 3-bromomercuri-D-camphor was carried out in the same way. 3,3'-Mercuribis-D-camphor after two recrystallizations from aqueous dioxan melted at 200-211° (decomp.).

5. Symmetrization of diastereomer (I) of 3-bromomercuri-L-camphor with sodium thiosulfate. 50 ml of water was poured over 10 g of 3-bromomercuri-L-camphor ($[\alpha]_D^{18}$- 29.5° ± 1.1°) and 50 ml of benzene was added. To this mixture was added dropwise, over a period of 30 minutes with vigorous stirring in the cold, an aqueous solution of 7.5 g of sodium thiosulfate (30% excess). After $1\frac{1}{2}$ hours' additional stirring, the benzene layer was separated and the benzene was evaporated to dryness. After repeated washing of the 3,3'-mercuribis-L-camphor with water and then with ether, 4.7 g of the compound (79%) was obtained with m.p. 195-210°. After recrystallization from 30% aqueous dioxan its m.p. was 229-232° (decomp.) and $[\alpha]_D^{18}$-165.9° ± 1.1° (c 1.76, l 1.9, α-3.75° ± 0.05°).

Found %: C 47.61, 47.77; H 6.03, 6.05. ($C_{10}H_{15}O)_2$ Hg. Calculated %: C 47.69; H 6.01.

6. Symmetrization of diastereomer (III) of 3-bromomercuri-D-camphor with sodium thiosulfate. From 8.0 g of 3-bromomercuri-D-camphor ($[\alpha]_D^{18}$ + 28.7° ± 1.2°) and 6.1 g of sodium thiosulfate (30 % excess) there was obtained under the conditions of the preceding experiment 3.5 g (75%) of 3,3'-mercuribis-D-camphor with m.p. 195-211°. After recrystallization from aqueous dioxan the m.p. was 229-232° and $[\alpha]_D^{18}$ + 163.5° ± 1.1° (c 3.07, l 1.9, α + 7.1 ± 0.05°).

7. Reaction of 3,3'-mercuribis-L-camphor (obtained by symmetrization of diastereomer (I) of 3-bromo-mercuri-L-camphor with sodium thiosulfate) with an equimolecular amount of hydrogen bromide. 1 g of un-recrystallized 3,3'-mercuribis-L-camphor, obtained by the symmetrization of diastereomer (I) of 3-bromomercuri-L-camphor ($[\alpha]_D^{18}$-29.5° ± 1.1°) with sodium thiosulfate, was dissolved in 25 ml of methyl alcohol. To this solution was added dropwise, with vigorous stirring in the cold over a period of 30 minutes, 4 ml of an alcoholic solution of hydrogen bromide containing 0.16 g HBr. The alcohol was evaporated to dryness and the dry residue was washed with ether and then dissolved again in 30 ml of hot dioxan. After the slight amount of insoluble precipitate had been filtered off, the dioxan was evaporated to dryness. The residue was washed with ether (5 ml). 0.62 g (74%) of 3-bromomercuri-L-camphor was obtained with m.p. 195-215°, $[\alpha]_D^{18}$ -38.8° ± 1.8° (c 1.46, l 1.9, α-1.10 ± 0.05°). After recrystallization from 60% aqueous dioxan, diastereomer (I) of 3-bromo-mercuri-L-camphor melted at 222-223°; $[\alpha]_D^{18}$ -31.6 ± 1.5° (c 1.91, l 1.9, α-1.15 ± 0.05°).

Found %: C 28.04; 28.72; H 3.48, 3.50. $C_{10}H_{15}$OHgBr. Calculated %: C 27.82; H 3.50.

8. Reaction of 3,3'-mercuribis-D-camphor (obtained by the symmetrization of diastereomer (III) of 3-bromomercuri-D-camphor with sodium thiosulfate) with an equimolecular amount of hydrogen bromide. 2 g of unrecrystallized mercuribis-D-camphor, obtained by the symmetrization of diastereomer (III) of 3-bromomercuri-D-camphor ($[\alpha]_D^{18}$ + 28.7° ± 1.2°) with sodium thiosulfate, was dissolved in 25 ml of methyl alcohol. To this solution was added dropwise, with vigorous stirring in the cold over a period of 30 minutes, 8 ml of an alcoholic solution of hydrogen bromide containing 0.32 g HBr. The alcohol was evaporated to dryness and the residue was washed with ether (5 ml) to remove camphor. 1.3 g (74% of 3-bromomercuri-D-camphor was obtained with m.p. 192-210°; $[\alpha]_D^{18}$ + 37.2° ± 2.07° (c 1.07, l 1.9, α + 0.7° ± 0.05°). After recrystallization from 60% aqueous dioxan, diastereomer (III) of 3-bromomercuri-D-camphor melted at 222-223°; $[\alpha]_D^{18}$ + 32.7° ± 2.0° (c 1.29, l 1.9, α + 0.8° ± 0.05°).

•3,3'-Mercuribiscamphor was first synthesized by Picon [4]; however, he did not analyze this compound.

Found %: C 27.87, 28.09; H 3.60, 3.57. $C_{10}H_{15}OHgBr$. Calculated %: C 27.82; H 3.50.

9. Change in the configuration on the α-carbon atoms upon heating 3,3'-mercuribis-L-camphor (obtained by the symmetrization of diastereomer (I) of 3-bromomercuri-L-camphor with sodium thiosulfate) in aqueous dioxan. 3 g of unrecrystallized 3,3'-mercuribis-L-camphor was dissolved in 30 ml of 30% aqueous dioxan. The solution was boiled for 2 hours, after which the compound was isolated by evaporation of the solvent.

a) 1 g of the material (after heating in the aqueous dioxan) was dissolved in 25 ml of methyl alcohol. To the solution was added dropwise, with vigorous stirring in the cold over a period of 30 minutes, 2.5 ml of an alcoholic solution of hydrogen bromide containing 0.016 g of HBr. The alcohol was evaporated and the dry residue was washed with water and ether. 0.6 g (72%) of 3-bromomercuri-L-camphor was obtained with m.p. 195-215°. After recrystallization from aqueous dioxan it melted at 217-219°, $[\alpha]_D^{18}$ -54.9° ± 1.4° (c 1.53, l 1.9, α -1.6° ± 0.05°).

b) 2 g of mercuribis-L-camphor (after heating in aqueous dioxan) was recrystallized from 25 ml of 30% aqueous dioxan. The compound had $[\alpha]_D^{18}$ -152.1° ± 1.3° (c 1.99, l 1.9, α -5.75° ± 0.05°). After a second recrystallization from 25 ml of 30% aqueous dioxan the value was $[\alpha]_D^{18}$ -220° ± 2.5° (c 1.05, l 1.9, α -4.4° ± ± 0.05°). After a third recrystallization from 25 ml of 30% aqueous dioxan it was $[\alpha]_D^{18}$ -236.6° ± 2.4° (c 1.05, l 1.9, α -4.85° ± 0.05°).

Thus, it is clear that 3,3'-mercuribiscamphor undergoes a change in configuration on the α-carbon atoms upon heating in aqueous dioxan and is converted into a mixture of the diastereomers.

SUMMARY

1. Both diastereomers of 3-bromomercuri-L-camphor and both diastereomers of 3-bromomercuri-D-camphor have been prepared.

2. The stereochemistry of the symmetrization reaction of the more stable diastereomers of 3-bromomercuri-L-camphor and 3-bromomercuri-D-camphor with sodium thiosulfate has been studied. It has been shown that in this reaction, which is an electrophilic substitution reaction on a saturated carbon atom, the configuration is preserved.

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MECHANISM OF THE CONVERSION OF o-TOLUENESULFONIC ACID
INTO p-TOLUENESULFONIC ACID

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In previous work [1] the question has been raised of the mechanism of migration of the sulfo group in the conversion of α-naphthalenesulfonic acid into β-naphthalenesulfonic acid. It has been shown that the sulfo group migrates intermolecularly, although in experiments with 94% sulfuric acid the results were somewhat unclear. Hollemann and Calland [2] investigated the conversion of o-toluenesulfonic acid into the para-isomer. These authors considered that the process takes place intramolecularly, and not through hydrolysis and subsequent sulfonation in the para-position. They showed that in this process there was no desulfonation because desulfonation occurs more slowly than rearrangement. Furthermore, sulfonation yields 4% of the meta-product, which was not detected by them in this reaction. E. A. Shilov and F. M. Vainshtein [3] investigated the transition of the ortho-isomer to the para-isomer at 120-126°, employing labeling with radioactive sulfur, S^{35}. They arrived at the conclusion that the conversion goes intermolecularly for the most part. In the work of these authors, however, it is indicated that the method used by them for separating the ortho- and para-isomers by the different solubility of their barium salts did not permit determining the specific radioactivity of the rearrangement products in the initial stage of the reaction. We have shown that for a more detailed explanation of the mechanism it is necessary to follow the conversion from the very beginning of the reaction, using not only the method of labeled atoms, but also another independent and sufficiently accurate method, such as the measurement of the absorption spectra.

In the present work we have attempted to trace the course of the conversion of o-toluenesulfonic acid to the para-isomer in different media with the aid of the radiochromatographic method in conjunction with spectrophotometry.

EXPERIMENTAL

To prepare the pure ortho-isomer, toluene was sulfonated with 96% sulfuric acid in a molar ratio of 1:5 at a temperature of 0°. After the toluene layer had disappeared, the mixture was poured into water, the p-toluenesulfonic acid hydrate was separated out, and the filtrate was neutralized with barium carbonate and concentrated. Separation of the isomers was carried out by means of their barium salts, which differ in their solubility in water [4]. By one recrystallization we succeeded in obtaining the pure barium salt of the ortho-isomer. To check the purity of the preparation, the salt was studied with the microscope and it also was converted through the potassium salt and the sulfonyl chloride to o-toluenesulfonamide with m.p. 155°, which agrees well with the data in the literature. p-Toluenesulfonic acid was prepared either by recrystallization, at 0° from concentrated hydrochloric acid, of the crude compound obtained as a side product in the preparation of the ortho-isomer, or by sulfonation of toluene with concentrated sulfuric acid [5]. The hydrate of pure p-toluenesulfonic acid melted at 104-105°.

We measured the ultraviolet-absorption spectra of the barium salts of the ortho- and para-isomers in an SF-4 photoelectric spectrophotometer. In the literature we found no data on the ultraviolet spectra of the isomers of toluenesulfonic acid, except for one publication [6] on the spectrum of the sodium salt of the ortho-isomer in water. The absorption curves for the barium salts of the ortho- and para-isomers in water differ substantially in the 2600-2800 A region and have an isobestic point at 2505 A (Fig. 1).
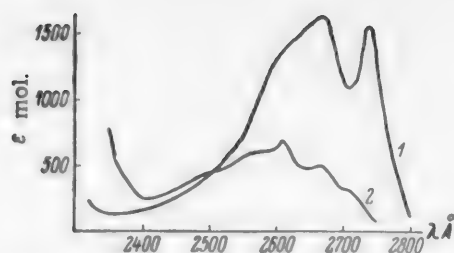
Fig. 1. Ultraviolet absorption spectra:
1) barium salt of o-toluenesulfonic acid; 2) barium salt of p-toluenesulfonic acid.

We checked how the pure solutions of the barium salts of the ortho- and para- isomers and their mixtures obeyed Beer's law in the concentration range 0.08-0.6 g / liter used by us in the spectrophotometric measurements. No deviations from Beer's law were noted. Using the data obtained on the intensity of absorption of the pure barium salts of the ortho- and para-isomers, we derived the following formula for calculating the percentage content of p-toluenesulfonic acid in a mixture of the isomers:

$$\left(1.422-0.382\,\frac{d^{2670}}{d^{2505}}\right)\cdot 100,$$

where d^{2670} and d^{2505} are the optical densities of the mixture at 2670 and 2505 A, respectively.
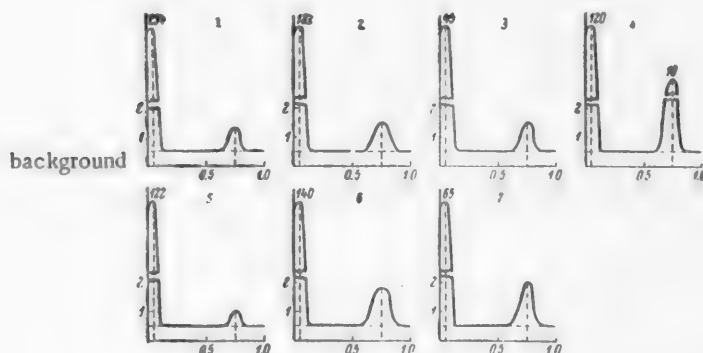

Fig. 2. Data from chromatographic analysis of mixtures of un-labeled o- or p-toluenesulfonic acid, H_2SO_4 and $Na_2S^{35}O_4$ after heating at 110°:
1) ortho-, 1-hour heating; 2) ortho-, 2 hours; 3) ortho-, 8 hours; 4) ortho-, 12 hours; 5) para-, 2 hours; 6) para-, 8 hours; 7) para-, 10 hours; ordinate, number of impulses per minute (1 division equals 64 impulses per minute); abscissa, R_f value; R_f of sulfate 0.05; R_f of o- and p-toluenesulfonic acid 0.75.

To clarify the mechanism of the conversion of o-toluenesulfonic acid to p-toluenesulfonic acid, we carried out three series of experiments. In the first series 0.5 g of o- or p-toluenesulfonic acid was heated in 1 ml of 95% sulfuric acid at 80 and 110° ± 1°. The proportions by weight of o- or p-toluenesulfonic acid, sulfuric acid, and water were 1: 3.5 : 0.2, and the molar proportions were 1: 6.2 : 2.1. In parallel tests, a solution of $Na_2S^{35}O_4$ with an activity of 200 μ C was first added to a test tube and evaporated to dryness. Then the ortho- or para- acid and H_2SO_4 were added to it in the above-mentioned proportions. After certain intervals of time a 1-ml sample was taken from the sulfo mixture and diluted with water. In the experiments where radioactive material was not added, the samples taken were neutralized with barium carbonate; the barium sulfate was separated out by centrifuging, and the filtrate, which contained the barium salts of the ortho- and para- isomers, was examined spectrophotometrically. In experiments where radioactive material was added, the samples taken were neutralized with sodium hydroxide to phenolphthalein, then 0.1 ml of the mixture was applied in series to a chromatogram . We used one-dimensional, descending chromatography on paper. Good separation of the sulfonic acid spots from the sulfate was obtained by using a mixture of butanol, pyridine, concentrated aqueous ammonia solution, and water in the proportions 40 : 40: 10: 30, and also with a mixture of methanol, concentrated

aqueous ammonia solution, and water in the proportions 80 : 10 : 10. After the separation was completed, when the solvent front had passed through 35-45 cm on the paper, the chromatogram was withdrawn from the chamber and dried. The radioactivity was determined along the course of the spots, one after another, over the length of the chromatogram, by means of an open-end counter covered with a lead plate with an aperture 1 x 2.5 cm. The results of the readings were plotted on a graph (radioactivity on the ordinate axis in imp / min. and R_f on the abscissa axis). The results of the chromatographic analysis of the experiments are presented in Fig. 2.

From the analysis of the chromatograms it can be seen that it was possible to separate the toluenesulfonic acids from the inorganic sulfate. The radioactive sulfate remained in place, and the o-and p-toluenesulfonic acids moved the same distance. A gradual intrusion of the radioactive sulfate from the medium into the ortho- and para- acids took place. The ratio of the activities of the spots of the sulfonic acids and of the sulfate on the chromatogram was determined by measurement of the areas under the curves on the graph. From the relation of the activities of the spots it was possible to estimate the degree of intrusion of the radioactive sulfate from the medium into the ortho- and para- isomers and the extent of intermolecular conversion. The degree of conversion was determined from the data of the radiochromatographic analysis with an accuracy of ± 3%. The total conversion independent of the mechanism was determined spectrophotometrically. The degree of conversion was measured by the ultraviolet absorption spectra with an accuracy of ± 0.5% The data on the conversion of the ortho-isomer to the para- isomer, and also on the reverse conversion, calculated from the spectra and the radiochromatographic analysis, were plotted on a graph where the ordinates were the percent of conversion and the abscissas the time in hours. In Fig. 3 are shown the results of the experiments at 110°.
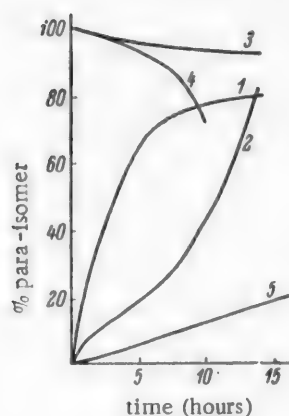

Fig. 3. Data on the reciprocal conversion of o- and p-toluenesulfonic acids at 110°: 1) ortho-to para- isomer in sulfuric acid medium (from UV spectra); 2) ortho- to para- isomer in sulfuric acid medium (from radiochromatographic analysis); 3) para- to ortho- isomer in sulfuric acid medium (from UV spectra); 4) para- to ortho-isomer in sulfuric acid medium (from radiochromatographic analysis); 5) ortho- to para-isomer in orthophosphoric acid medium (from UV spectra).

As can be seen, the total conversion does not coincide with the intermolecular. The sulfo group migrates from the ortho- to the para- position not only according to the intermolecular mechanism, but also intramolecularly. Thus, for example, in two hours the total conversion is 36%, but that by the intermolecular mechanism is only 10%. Consequently, the intramolecular conversion in this time amounts to 26% Only in a condition close to equilibrium do the two curves coincide. When the para- isomer is converted to the ortho- isomer, the process proceeds considerably more slowly. In this case the hydrolysis of the sulfo group with subsequent resulfonation to the more stable position, namely to the same para-position, results mainly in exchange with the medium, and not conversion of the para- isomer to the ortho-isomer. The curve calculated from the radiochromatographic analytical data lies wholly below the curve calculated from the ultraviolet spectra. At 80° (Fig. 4), where the rate of conversion is considerably less, the same differences are observed. The sulfo group migrates to the para-position both intramolecularly and intermolecularly. It is interesting to note that the intramolecular conversion outstrips the exchange reaction to a particularly great extent in the first hours of the experiment.

In the second series of experiments o- toluenesulfonic acid was heated at 110° in 77% H_3PO_4 The proportions by weight of o- toluenesulfonic acid, H_3PO_4, and H_2O were 1: 18: 5.5, and the molar porportions were 1:31.6: :52.5. After certain intervals of time, 1-ml samples were taken, which were treated as in the first series and then subjected to spectrophotometric examination. In 8 hours the para- isomer content amounted to 11%, in 16 hours it was 20%, and in 32 hours it was 31% It might be supposed that in H_3PO_4 medium the sulfo group completely splits off and the sulfuric acid forms sulfonates in the para- position. However, in this case the concentration of sulfuric acid would be 2.5% Spectrophotometric analysis showed that the concentration of ortho-isomer decreases during the reaction, apparently as a result of hydrolysis. In 8 hours hydrolysis proceeds to the extent of 32%, in 16 hours 56%, and in 32 hours 65%. Thus, in 8 hours the concentration of para- isomer amounts to 7.5% of the initial concentration of ortho- isomer, in 16 hours 8.8%, and in 32 hours 10.4%
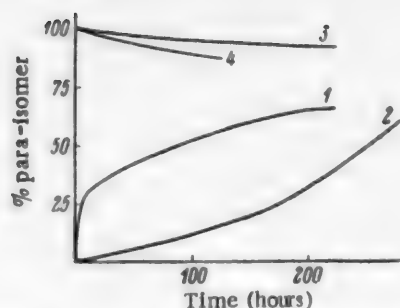
Fig. 4. Data on reciprocal conversion of o- and p-toluenesulfonic acids at 80°. 1) ortho- to para- isomer in sulfuric acid medium (from UV spectra); 2) ortho- to para- isomer in sulfuric acid medium (from radiochromatographic analysis); 3) para- to ortho-isomer in sulfuric acid medium (from UV spectra); 4) para- to ortho- isomer in sulfuric acid medium (from radio - chromatographic analysis).

In a third series of experiments 0.13 g of the barium salt of ortho-toluenesulfonic acid was dissolved in 5 ml of anhydrous glycerin and heated at 110° for 214 hours. Spectrophotometric analysis showed the absence of any change in the starting material.

Thus, our experiments show that in the first hours of the reaction, rearrangement proceeds intramolecularly to a considerable degree. Hydrolysis and resulfonation further lead to a shift of the sulfo group by the intermolecular mechanism also, and the specific radioactivity of the rearrangement product becomes equal to the specific radioactivity of the sulfo mixture at the moment of equilibrium. We should note that in a recently published study by F. M. Vainshtein and E. A. Shilov [7] devoted to the mechanism of rearrangement of α-naphthalenesulfonic acid to the β-isomer it was found that the process takes place intramolecularly in part (20-30 %).

DISCUSSION OF RESULTS

Intermolecular reaction. As our experiments show, the ortho-para conversion proceeds through the medium, i.e. intermolecularly, apparently through desulfonation and subsequent resulfonation in the para-position. We think that this reaction proceeds through cyclic active complexes. We point out that an exchange of hydrogen between benzene and deuterated sulfuric acid, in all probability, takes place in a similar way (1).

$$\text{(1)}$$
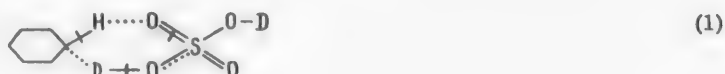
A six-membered active complex is more likely than a four-membered one because oxygen in the S = O bond is much more polar than oxygen in the S-O-H bond. This contributes to easier breaking away of the hydrogen from the benzene. In this connection it may be thought that in sulfonation the splitting off of hydrogen is not the limiting stage, as it is in the nitration of aromatic compounds. The authors who have investigated the mechanism of sulfonation indicate the essential significance of sulfur trioxide [8]. E. A. Shilov [9] first proposed a six-membered, cyclic active complex with SO_3 participating, according to diagram (2).

$$\text{(2)}$$

Under conditions where the experiment is carried out in strong sulfuric acid solution, the sulfonating agent is the solvate SO_3 molecule. The condition of the SO_3 in solution can be represented in the form of an ion pair $\overset{+}{HSO_3} \ldots \overline{HSO_4}$ or $H_2S_2O_7$, which is obtained by scheme (3).

$$O_2S \underset{O \rightleftharpoons SO_2H}{\overset{O \cdots H}{\rightleftharpoons}} O \longrightarrow H_2S_2O_7 \longrightarrow \overset{+}{HSO_3} \cdots \overline{HSO_4} \qquad \text{(3)}$$

It is material that the ions $\overset{+}{HSO_3}$ and $\overline{HSO_4}$ can form in strong sulfuric acid also as the result of another reaction (4).

$$2H_2SO_4 \longrightarrow H_3SO_4^+ + H\overline{S}O_4 \qquad\qquad (4)$$
$$\downarrow$$
$$HSO_3^+ + H_2O$$

This explains the fact that sulfur trioxide promotes the reaction, but is not a necessary condition for its occurrence. The active complex in sulfonation can be represented by diagram (5).

(5)
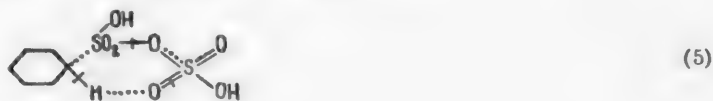
At the same time, as indicated above, the splitting out of hydrogen does not limit the reaction. On the principle of microscopic reversibility, desulfonation also goes according to diagram (5). The subsequent sulfonation by virtue of kinetic principles goes predominantly in the para-position.

Intramolecular migration of the sulfo group. Conversion of the ortho- isomer to the para- isomer without the participation of the medium might take place as a result of bimolecular reaction of two molecules of o-toluenesulfonic acid with redistribution of the two sulfo groups and two atoms of hydrogen. However, such a complex rearrangement at one stroke is very improbable, particularly on steric principles.

In our work it has been shown that the process goes intramolecularly to a considerable extent. The question arises as to the detailed mechanism of this reaction. Dewar [10] assumed the formation of a complex according to scheme (6).

(6)
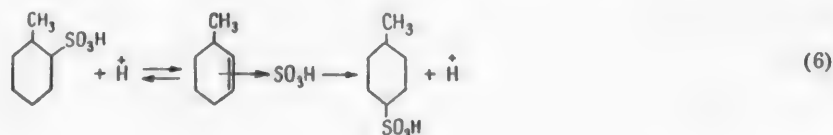
In the π-complex hypothesis it is assumed that the electron pair of the π-bond manifests donor properties relative to the positive ion or group, which are acceptors. An isolated π-bond in a number of instances actually shows such donor properties to a considerable degree. We point out, for example, that the dielectric polarization of iodine in cyclohexane is $31\,cm^3$, while in cyclohexene it is $56\,cm.^3$ This is connected, no doubt, with the formation of a strongly polarized π-complex. But the π-bonds of the benzene ring are not capable of yielding significantly polarized π-complexes, first of all because in benzene there are no isolated π-bonds and the six electrons move into a field of six centers. Actually, the dielectric polarization of iodine in benzene is $39\,cm^3$, i.e., very much less than in cyclohexene. Furthermore, in the framework of ideas of the usual π-complex it is not clear why the sulfo group on the way from the ortho-position to the para passes up the meta- position.

In connection with this, we think of the structure of the intermediate complex in the migration process somewhat differently. The necessity of an acid medium for the transfer of the sulfo group can be explained by the fact that the group adds a proton and reacts in form (7).

(7)

If we consider that the S=O bond is strongly polar, then it is easy to see that sulfur in the protonated sulfo group carries a considerable positive charge (8).

(8)

This promotes the strengthening of the acceptor properties of the sulfur in relation to the π-electrons. We further think that in the process of migration, the sulfo group is bound not with any one π-bond, because of the absence in benzene of isolated π-bonds, but with the whole system of π-electrons of benzene. It is possible that in migration the sulfo group is bound chiefly with the ortho- and para-positions, inasmuch as these positions, in the benzene ring because of the presence of the CH_3 group, are the places with an increased electron density. If so, then in the active complex, the $SO_3H_2^+$ group is located under the plane of the benzene ring with a sulfur atom which is on the perpendicular dropped from the center of the ring to its plane, as can be seen from diagram (9).
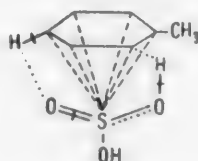
$$(9)$$

Because of such a configuration, the sulfo group can most easily migrate either to the other ortho-position or to the para-position. Combination in an active complex by reaction with the π-electron system of the benzene ring contributes to lowering the energy of activation. We were not able to determine with sufficient accuracy the energy of activation of intramolecular conversion. In any case, for the initial stage of the reaction, far from equilibrium, calculation by the equation for a unimolecular reaction with an exponent of the order of 10^{13} shows that the energy of activation does not exceed 30 kcal. In the reaction process, as can be seen from the structure of the active complex, the C—S, C—H, and O—H bonds and the S=O π-bond break. In their place appear new C—S, C—H, O—H, and S = O π-bonds. When polar bonds are present, such a redistribution represents the process with the least structural changes and the lowest energy barrier. In the reaction, the protonated sulfo group probably gives up its hydrogen to the carbon that previously was bound with the sulfur (the ortho-carbon). At the same time the hydrogen from the para-position becomes bound with the oxygen of the S=O group, and in the vacant place on the para-carbon a new bond with sulfur appears.

We think that similar mechanisms with the formation of intermediate complexes in which reaction occurs with all the π-bonds of the benzene ring are characteristic of a number of Jacobsen reactions and other intramolecular migrations.

SUMMARY

1. The mechanism of conversion of o-toluenesulfonic acid to the para-isomer has been investigated by a radiochromatographic method using radioactive S^{35} and by an independent spectrophotometric method (ultraviolet-absorption spectra).

2. It has been found that in acid medium the process proceeds intramolecularly to a considerable extent. The reaction also goes partially by way of the medium; i.e., intermolecularly.

3. The intermolecular reaction can be represented as the result of the formation of a six-membered, cyclic active complex.

4. To explain the intramolecular reaction, it has been suggested that an active complex is formed in which the sulfur of the sulfo group is located under the plane of the benzene ring at an equal distance from all the carbon atoms and reacts with all the π-electrons of the ring.

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INVESTIGATION IN THE FIELD OF SUBSTITUTED
1,5-DIPHENYLTHIOCARBAZONES

VII. THE EFFECT OF THE NATURE OF SUBSTITUENTS IN THE BENZENE RINGS OF 1,5-DIPHENYLTHIOCARBAZONES ON THE THIONE—THIOL TAUTOMERIC EQUILIBRIUM

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In previous papers, we have shown that 1,5-diphenylthiocarbazones exist in solutions as a mixture of the two tautomers thione and thiol. Moreover, the long wave-length maximum on the absorption curve belongs to the thione form [1]. Further, it was demonstrated [2] that the ratio of the intensity in the band containing the long wave-length maximum $d\lambda_{max_2}$ to the intensity in the band containing the short wave-length maximum $d\lambda_{max_1}$ is equal to the tautomeric thione-thiol equilibrium constant.

$$K_{\tau} = \frac{d_{\lambda_{max_2}}}{d_{\lambda_{max_1}}}.$$

Further, the effect of the solvent on the tautomeric equilibrium was studied in the arylthiocarbazone series, and it was shown that polar solvents shift the equilibrium toward the thiol side [1].

It is well known that many investigations have been devoted to the question of the dependence of keto-enol tautomeric equilibria on the structure of the tautomerizing compounds. However, there have been but few such investigations in the field of thione-thiol tautomers, and there are none in the field of arylthiocarbazones. Therefore, it was of interest to trace the effect of substitutents in the benzene rings of arylthiocarbazones on the thione-thiol tautomeric equilibrium in solution.

The synthesis of arylthiocarbazones has been described by us previously [3,4]. Data from the spectrophotometric investigation of arylthiocarbazones are presented in the table. It may be concluded from these data that for thiocarbazones in which the benzene rings have an electron-donor substituent, the extinction in the band containing the long wave-length maximum is higher than the extinction for the short wave-length maximum (preparations nos. 13-32). For thiocarbazones containing electron-acceptor substituents in the benzene rings, on the other hand, the extinction in the band containing the short wave-length maximum is equal to or even greater than the extinction in the band containing the long wave-length maximum (preparations nos. 1-12). This is shown graphically in Figure 1, where absorption curves are presented for two arylthiocarbazones with electron-donor substituents, three with electron-acceptor substituents, and the absorption curve for 1,5-diphenylthiocarbazone. The α- and β-naphthylthiocarbazones (preparations nos. 33 and 34) are especially interesting from this point of view. In view of the very poor solubility in benzene, the absorption spectra of these compounds were taken in carbon tetrachloride. Our data are in agreement with the data of Hubbard [5] (chloroform solvent). For these two thiocarbazones, there was no maximum in the visible region of the spectrum. The introduction of bromine into the naphthylene nucleus (preparation no 35) caused the appearance of a maximum in the short wave-length region. The introduction of a nitro group gave a compound having only one absorption maximum, at 550 m_μ (preparation no. 36). Thus, electron-donor substituents in the benzene rings of 1,5-diphenylthiocarbazones have the same effect on the ratio of thione and thiol forms of the thiocarbazones as polar solvents — methyl alcohol, formamide, and others [1].

Prep. No.	R	λmax_1 (in mμ)	λmax_2 (in mμ)	$d\lambda max_1$	$d\lambda max_2$	$\dfrac{d\lambda max_2}{d\lambda max_1}$	Solvent
1	4-COOHC$_6$H$_4$	460	640	1.82	1.32	0.72	Acetone
2	4-CH$_3$COC$_6$H$_4$	455	650	1.9	1.5	0.79	Chloroform
3	4-FC$_6$H$_4$	445	620	1.62	1.30	0.8	Acetone
4	2,4-Cl$_2$C$_6$H$_3$	455	655	2.08	1.67	0.8	
5	2,4-I$_2$C$_6$H$_3$	470	675	1.84	1.54	0.82	
6	3-IC$_6$H$_4$	455	645	1.65	1.51	0.92	
7	4-IC$_6$H$_4$	460	660	2.16	2.14	0.99	
8	2,4-Br$_2$C$_6$H$_3$	445	645	1.3	1.29	0.99	
9	4-C$_6$H$_5$COC$_6$H$_4$	450	655	2.32	2.32	1.0	
10	4-ClC$_6$H$_4$	452	626	1.24	1.25	1.0	
11	2-IC$_6$H$_4$	475	655	2.82	2.86	1.01	
12	3-ClC$_6$H$_4$	460	631	1.00	1.02	1.02	
13	4-CF$_3$SC$_6$H$_4$	450	640	6.24	6.8	1.1	
14	2-ClC$_6$H$_4$	465	645	1.4	1.58	1.11	
15	4-COOC$_2$H$_5$C$_6$H$_4$	470	650	1.57	1.80	1.14	
16	4-SO$_2$NH$_2$C$_6$H$_4$	465	640	0.89	1.25	1.14	
17	4-C$_6$H$_5$NHC$_6$H$_4$	450	630	4.72	7.68	1.63	Benzene
18	C$_6$H$_5$	450	620	1.6	2.8	1.75	
19	4-CH$_3$SC$_6$H$_4$	530	675	4.2	7.56	1.8	
20	4-C$_6$H$_5$C$_6$H$_4$	480	655	2.8	5.4	1.93	
21	3-CH$_3$C$_6$H$_4$	465	635	2.05	4.28	2.09	
22	4-n-C$_4$H$_9$C$_6$H$_4$	455	635	3.16	6.68	2.12	
23	4-C$_2$H$_5$C$_6$H$_4$	445	635	2.8	4.24	2.14	
24	2-C$_2$H$_5$C$_6$H$_4$	465	635	1.68	3.6	2.14	
25	4-CH$_3$C$_6$H$_4$	465	630	2.4	5.4	2.25	
26	4-(CH$_3$)$_2$CHC$_6$H$_4$	455	630	2.32	5.24	2.25	
27	2-C$_6$H$_5$OC$_6$H$_4$	480	650	2.1	4.87	2.32	
28	2-CH$_3$OC$_6$H$_4$	486	659	2.72	6.36	2.34	
29	2-CH$_3$C$_6$H$_4$	470	632	1.8	4.6	2.56	
30	β-tetralin	465	635	3.56	10.08	2.83	
31	4-CH$_3$OC$_6$H$_4$	476	646	2.55	7.55	2.96	
32	4-CH$_3$CONHC$_6$H$_4$	460	658	1.48	4.48	3.03	Acetone
33	β-C$_{10}$H$_7$	—	662	...	4.9		Carbon tetrachloride
34	α-C$_{10}$H$_7$		683		5.4		Carbon tetrachloride
35	5-BrC$_{10}$H$_6$	490	675	1.84	5.84	3.17	Chloroform
36	4-NO$_2$C$_6$H$_4$	550	—	2.02			Acetone

It should be emphasized that thiocarbazones for which the short wave-length maximum on the absorption curve is weak or entirely absent (preparations nos. 12-35), i.e., those for which the thiol form exists to an insignificant extent or not at all, are less soluble in aqueous alkali, form inner complex salts with heavy metals at higher pH, and are more stable toward oxidation.

It can be assumed that withdrawal of electrons along the system of conjugated bonds from the thiocarbazone group toward the electron-acceptor substituent in the benzene rings facilitates the migration of the hydrogen atom from the nitrogen to the sulfur. This finds outward expression in the regions of both maxima. The shift of electrons from the substituent in the benzene rings along the system of conjugated bonds toward the thiocarbazone group hinders the migration of hydrogen; i.e., in these cases, the possibility of conversion to the thiol form is decreased, and this finds its outward expression in the greater intensity of the long wave-length maximum of the thiocarbazones.

The spectrophotometric investigation of the arylthiocarbazones in the ultraviolet showed that there is an additional small maximum lying in the range of 290-360 mμ on the absorption curves of the dithizones. As seen from Figure 2, for derivatives of dithizone with electron-acceptor substituents these maxima are shifted

toward the longer waves, with respect to the maxima of dithizone and its derivatives with electron-donor substituents. The question of the character of this maximum on the absorption curves of arylthiocarbazones will be discussed in a separate article.
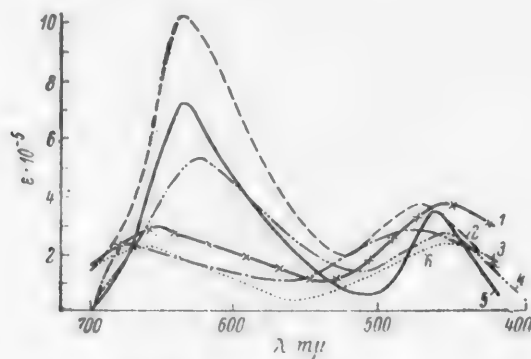

Fig.1. Absorption spectra. 1) 1,5-di-(4-acetophenyl)
thiocarbazone, 2) 1,5-di-(tetrahydro-β-naphthyl)thio-
carbazone, 3) 1,5-di-(2,4-diiodophenyl)thiocarbazone,
4) 1,5-diphenyl-thiocarbazone, 5) 1,5-di(4-tolyl)thio-
carbazone, 6) 1,5-di(4-benzophenyl)thiocarbazone.
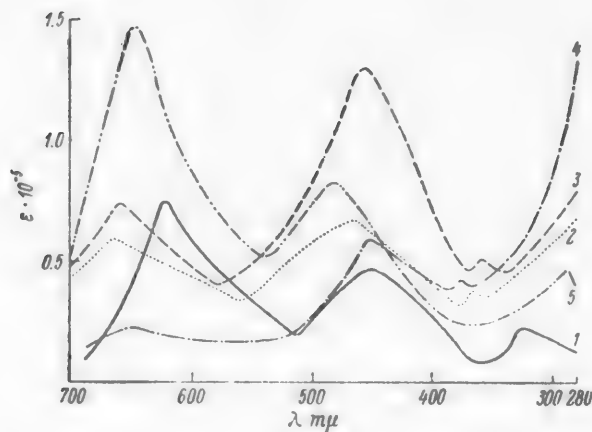
Fig. 2. Absorption spectra. 1) 1,5-diphenylthiocarbazone,
2) 1,5-di(2,4-diiodophenyl)thiocarbazone, 3) 1,5-di(2,4-
dichlorophenyl)thiocarbazone, 4) 1,5-di(4-acetophenyl)
thiocarbazone, 5) 1,5-di(2-phenoxyphenyl)-thiocarbazone.

SUMMARY

1. A spectrophotometric investigation of 36 substituted 1,5-diphenylthiocarbazones was carried out.

2. The effect of the nature of substituents in the benzene rings of 1,5-diphenylthiocarbazone on the thione-thiol tautomeric equilibrium was studied.

3. It was shown that electron-acceptor substitutents shift the thione-thiol tautomeric equilibrium of substituted 1,5-diphenylthiocarbazones toward the thiol form.

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INVESTIGATIONS IN THE SERIES OF SUBSTITUTED 5-HYDROXY-2,3-DIPHENYLTETRAZOLIUM BETAINES

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For some time past, various quaternary ammonium derivatives have been intensively studied as invert soaps, and their bactericidal properties have also been investigated [1]. Different tetrazolium compounds have been studied in this connection. During the synthesis of arylthiocarbazones by the formazyl method [2, 3], we obtained various substituted 1,5-diphenyl-3-nitroformazans as intermediate products. As shown by Pechmann and Runge [4], formazyl compounds can be converted by oxidation into tetrazolium derivatives or into the corresponding betaine-like compounds [5] according to the scheme:

$$O_2N-C\underset{N-NHR}{\overset{N=NR}{\big<}} + CH_3COOH \rightarrow HO-C\underset{N-NHR}{\overset{N=NR}{\big<}} + CH_3ONO_2 \xrightarrow{O}$$

$$\rightarrow C\underset{\underset{\underset{O^-}{\big|}}{N=NR}}{\overset{N-NR}{\big<}} \quad \text{or} \quad \bar{O}-C\underset{N-NR}{\overset{N=\overset{+}{N}R}{\big<}}$$

(I)
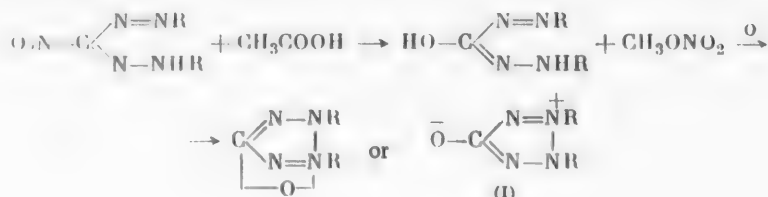
The oxidation or dehydrocyclization is carried out with the aid of yellow mercuric oxide or with amyl nitrite in an alcoholic solution of hydrogen chloride [4]. Recently, the oxidation of formazans has been carried out, with good yields, by means of lead tetraacetate in chloroform [1]. Wedekind and Stauve showed that the tendency toward ring closure to the tetrazole ring of substituted formazyl derivatives depends on the nature of the substituents in the 3-position and also on the nature and location of substituents in the benzene rings [6]. Bamberger, Padova and Ormerod studied the dehydrocyclization of 1,5-diphenyl-3-nitroformazan by heating in acetic acid in the presence of amyl nitrite; in this case, acidolysis of the nitro group occurs with subsequent oxidation of the nitroformazan to the tetrazolium derivative [7]. We have carried out the dehydrocyclization of nine different substituted 1,5-diphenyl-3-nitroformazans under these same conditions. In these studies, it was found that the meta- and para-substituted derivatives can undergo dehydrocyclization to tetrazolium derivatives in good yields, while the ortho-substituted compounds under these conditions either do not dehydrocyclize at all or do so with very insignificant yields. In the table are presented the synthesized substituted 5-hydroxy-2,3-diphenyltetrazolium betaines, which have the general formula (I).

The substituted 5-hydroxy-2,3-diphenyltetrazolium betaines are colorless or light-yellow crystalline materials. They may be crystallized from water. They are difficultly soluble in organic solvents and slightly soluble in alcohol. The substances decompose during melting, sometimes explosively. In the figure are presented the absorption curves of four preparations in alcohol in a concentration of $6.6 \cdot 10^{-5}$ M.

Substituted 5-Hydroxy-2,3-Diphenyltetrazolium Betaines (I).

R	Yield (in %)	Melting point	Maximum (in mμ)	Maximum (in mμ)	Empirical formula	N (in %) Found	calc.
p-CH$_3$C$_6$H$_4$	68	160°	235 330	230 290	C$_{15}$H$_{14}$ON$_4$	20.74, 20.8	21.05
m,p-(CH$_3$)$_2$C$_6$H$_3$	67	160	234 327	227 290	C$_{17}$H$_{18}$ON$_4$	18.79, 18.81	19.05
p-C$_2$H$_5$OC$_6$H$_4$	76	146	233 279 336	260 305	C$_{17}$H$_{18}$O$_3$N$_4$	16.76, 16.77	17.17
m-C$_2$H$_5$OC$_6$H$_4$	77	163	323	305	C$_{17}$H$_{18}$O$_3$N$_4$	17.15, 17.08	17.17
p-n.-C$_4$H$_9$OC$_6$H$_4$	54	137	229 275 333	265 305	C$_{21}$H$_{26}$O$_3$N$_4$	14.58, 14.42	14.66
p-iso-C$_5$H$_{11}$OC$_6$H$_4$	57	135	231 280 335	260 305	C$_{23}$H$_{30}$O$_3$N$_4$	13.33, 13.28	13.66
p-C$_2$H$_5$OOCC$_6$H$_4$	43	146	225 343	300	C$_{19}$H$_{18}$O$_5$N$_4$	14.48, 14.3	14.66
p-BrC$_6$H$_4$	54	160	245 335	235 295	C$_{13}$H$_8$ON$_4$Br$_2$	13.82, 13.88	14.14
p-COOHC$_6$H$_4$	45	176	225 336	305	C$_{15}$H$_{10}$O$_5$N$_4$	16.74, 16.79	17.17

Absorption spectra. 1) 5-Hydroxy-2,3-di(3,4-dimethylphenyl)tetrazolium betaine, 2) 5-hydroxy-2,3-di(4-tolyl)tetrazolium betaine, 3) 5-hydroxy-2,3-di(isoamyloxyphenyl) tetrazolium betaine, 4) 5-hydroxy-2,3-di(4-bromophenyl)tetrazolium betaine.

EXPERIMENTAL

The initial nitroformazyl derivatives used in the preparations of the compounds presented in the table were described by us previously [2, 3].

5-Hydroxy-2,3-di(3,4-dimethylphenyl)tetrazolium betaine. 18 g of 5-nitro-2,3-di(3,4-methylphenyl) formazan was suspended in a mixture of 40 ml of acetone, 14 ml of glacial acetic acid, and 7.5 ml of amyl nitrite. The mixture was refluxed 5 hours until the dark-red color had turned orange-yellow. The acetone was distilled on a water bath until the reaction mixture was half the original volume. Ether was added to the cooled solution, and the tetrazolium betaine derivative separated as a yellow, crystalline precipitate. Recrystallization of the resulting 5-hydroxy-2,3-di(3,4-dimethylphenyl) tetrazolium betaine from water with carbon gave pale-yellow, acicular crystals. The compound melted with explosive decomposition. The yield was 11g (67.5%).

The remaining tetrazolium betaine derivatives were synthesized under analogous conditions.

5-Hydroxy-2,3-(4-tolyl)tetrazolium betaine. 5 g of 5-nitro-2,3-di(4-tolyl) formazan was used in the reaction. Recrystallization from water with carbon gave light-orange crystals.

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5-Hydroxy-2,3-di(4-phenetyl)tetrazolium betaine. 10 g of 5-nitro-2,3-di(4-phenetyl)formazan was used in the reaction. The resulting tetrazolium betaine was purified by recrystallization from water with carbon.

5-Hydroxy-2, 3-di(3-phenetyl)tetrazolium betaine. 8.5 g of 5-nitro-2,3-di(3-phenetyl)formazan was used in the reaction. Recrystallization of the tetrazolium betaine from water with carbon gave white crystals. The compound melted explosively.

5-Hydroxy-2,3-di(4-n-butoxyphenyl)tetrazolium betaine. 2 g of the nitroformazyl derivative was used. Precipitation of the tetrazolium betaine from acetone solution by means of ether gave bright-yellow crystals. These were filtered and washed with alcohol and ether.

5-Hydroxy-2,3-di (4-isoamyloxyphenyl)tetrazolium betaine. 1.5 g of the nitroformazyl derivative was used. Precipitation with ether gave bright-yellow crystals of the tetrazolium betaine.

5-Hydroxy-2,3-di (4-carbethoxyphenyl)tetrazolium betaine. 2 g of 5-nitro-2,3-(4-carbethoxyphenyl)tetrazolium betaine was used. The tetrazolium betaine was obtained as pale-yellow crystals. The compound melted explosively.

5-Hydroxy-2,3-di(bromophenyl)tetrazolium betaine. 2 g of the nitroformazyl derivative was used. Precipitation with ether from an acetone solution gave a yellow crystalline material. The crystals were filtered and washed with alcohol and ether.

5-Hydroxy-2,3-di(4-carboxyphenyl)tetrazolium betaine. 1 g of 5-nitro-2,3-di(4-carboxyphenyl)formazan was used. The resulting tetrazolium betaine was purified by recrystallization from water with carbon. The product separated in the form of crystals with a pale-rose color. The compound melted explosively.

SUMMARY

Nine new, previously undescribed derivatives of 5-hydroxy-2,3-diphenyltetrazolium betaine were synthesized, and their absorption spectra were studied.

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•Original Russian pagination. See C. B. translation.

INVESTIGATIONS IN THE FIELD OF QUINOLINE AND ITS DERIVATIVES

XXI CONJUNCT CONDENSATION OF ARYLAMINES WITH HYDRACRYLALDEHYDE

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It has previously been pointed out that hydracrylaldehyde (β-hydroxypropionaldehyde) can participate together with acrolein in the Skraup reaction [1]. Indeed, it is formed in significant amounts both during the decomposition of glycerin [2] and during the addition of water to acrolein at elevated temperature [3], the addition reaction being catalyzed by acid [4]. In connection with this, it was of interest to study the interaction of certain aromatic amines with hydracrylaldehyde with the aim of obtaining quinolines. With the exception of a patent to Chichibabin*[5], this reaction has not been described in the chemical literature.

We have established that under the usual conditions of the Skraup synthesis, namely, the dropwise addition of hydracrylaldehyde to the reaction mixture at 120-140°, quinoline is obtained in a yield of 15 %. If milder conditions are used, m-nitrobenzenesulfonic acid as the oxidizing agent and a dilute solution as the reaction medium, the yield of quinolines resulting from the use of hydracrylaldehyde reaches 50%. This permits the conclusion that when the Skraup reaction is carried out with glycerin in the usual manner, and also when acrolein is substituted for glycerin [6], one course of the reaction is interaction with hydracrylaldehyde formed from the glycerin or acrolein.

The reaction of hydracrylaldehyde with aromatic amines is now extended to diarylamines. Thus, from diphenylamine we were able to obtain a salt of N-phenylquinoline, and this reaction has been applied to other diarylamines. In this manner, it has been shown that it is possible to introduce secondary amines into a modification of the Skraup synthesis with hydracrylaldehyde.

Of the several possible courses of the reaction of hydracrylaldehyde with arylamines leading to the formation of quinolines, the most probable is that represented by a scheme in which the anil of hydracrylaldehyde is converted to the anil of acrolein, which then cyclizes to the quinoline

$R = H, C_6H_5; \quad X = HSO_4.$

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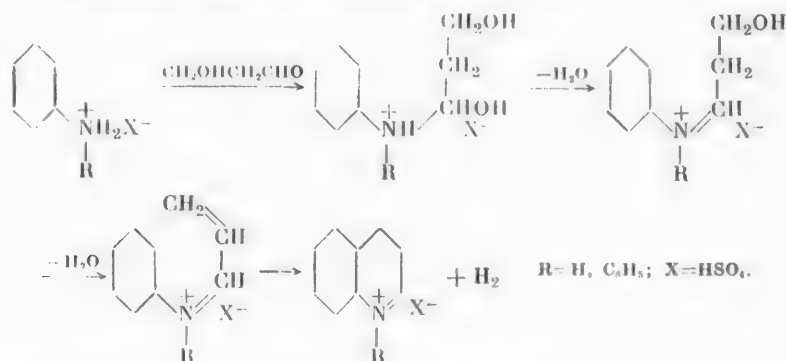
*The French spelling of the name is Tchitchibabine — Publisher's note.

Literature sources relating to the study of the mechanism of the Skraup reaction * and the experimental data obtained in the present work lead us to the conclusion that the Skraup reaction proceeds both through interaction with acrolein and through interaction with hydracrylaldehyde and, probably, glyceraldehyde **, and any of these courses can predominate depending on the starting products and on the conditions used.

EXPERIMENTAL

The reactions were carried out in a three-necked flask fitted with a stirrer, a thermometer, and a reflux condenser in which was inserted a dropping funnel. The first experiments were carried out using hydracrylaldehyde itself, but later, in view of the fact that the results were identical, the diethyl acetal of the ethyl ether of hydracrylaldehyde was used, since it was more readily available [5]. In order to avoid excessive tarring and decreased yields, the aldehyde components were always twice-rectified, and the product boiling at 91-92° at 32 mm was used.

Experiment 1. Quinoline. 9.3 g of aniline was added to 25 ml of H_2SO_4 (d . 1.84) and 12.5 g of nitrobenzene. The mixture was heated to 120°, and 17 g of the diethyl acetal of β -ethoxypropionaldehyde was added dropwise over the course of 0.5 hour; during the addition, the temperature did not rise above 130°. After this, the mixture was refluxed for an additional 1-2 hours at 138-148°. The quinoline was separated with potassium ferrocyanide [8]. The yield was 2.05 g (15.6%). B.p. 234-240°; m.p. of picrate, 201°.

Experiment 2. Quinoline. A solution of m-nitrobenzenesulfonic acid was prepared by Utermohlen's method [9] from 12.5 g of nitrobenzene, 50 g of 20% oleum, and 20 ml of water. 9.3 g of aniline was added to the solution; then, at 125-135° and over the course of 30-45 minutes, 20 g of the diethyl acetal of β -ethoxypropionaldehyde was added dropwise, after which the mixture was heated at 135-145° for another 1-1.5 hours. The yield of quinoline was 6.95 g (53.8%). B.p. 233-238°; m.p. of picrate, 200°.

Experiment 3. 6-Methoxyquinoline. This experiment was carried out similarly to Experiment 2. 6.74 g (43.4%) of 6-methoxyquinoline was obtained from 12.3 g of p-anisidine. B.p. 278-284°; m.p. of picrate, 212°.

Experiment 4. N-Phenylquinolinium perchlorate. 10 g of the diethyl acetal of β -ethoxypropionaldehyde was added, at a temperature of 120-130° and over the course of 15 minutes, to a mixture of 8.5 g of diphenylamine, 45 g of nitrobenzene, and 10 ml of H_2SO_4, and the mixture was heated for another 2 hours at 125-135°. The product was separated in a manner similar to that used for the isolation of N-arylquinaldinium salts [10]. The yield of perchlorate was 1.72 g (11.2%). Recrystallization from water gave a product with an m.p. of 157°.

Found %: C 58.75; H 3.79; Cl 11.83; ClO_4 33.78. $C_{15}H_{12}NClO_4$. Calculated %: C 58.93; H 3.95; Cl 11.60; ClO_4 32.69.

SUMMARY

1. Quinoline derivatives were obtained by the reaction of hydracrylaldehyde with anilines.

2. It was shown that it is possible to introduce diarylamines into the Skraup reaction. N-Phenylquinolium perchlorate was synthesized.

3. The mechanism of the reaction was discussed, and a scheme was proposed for the reaction.

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*For example, Jale pointed out that when acrolein is similarly used, only traces of quinoline are formed [7].
* *We are presently investigating this course of the reaction

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*Transliteration of Russian — Publisher's note.
 **Original Russian pagination. See C. B. translation.

INVESTIGATIONS IN THE FIELD OF ISOQUINOLINECARBOXYLIC ACIDS

III. PREPARATION OF A SERIES OF 1-ALKOXY-SUBSTITUTED ACIDS OF THE ISOQUINOLINE GROUP, THEIR ESTERS AND HYDRAZIDES, AND SOME DATA ON THE MOBILITY OF ALKOXY GROUPS ON THE ISOQUINOLINE RING

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The aim of the present investigation was to develop a synthesis for a series of trialkoxy-substituted acids of the isoquinoline group and certain of their derivatives, the testing of the physiological activity of which is of interest. We previously reported on the preparation of the chloride (I) and esters (II-V) of 1-chloro-7,8-dimethoxy-3-isoquinolinecarboxylic acid from the readily available opianic acid [1,2]. We used these substances for the preparation of a number of previously undescribed alkoxy-substituted acids of the isoquinoline series and some of their derivatives.
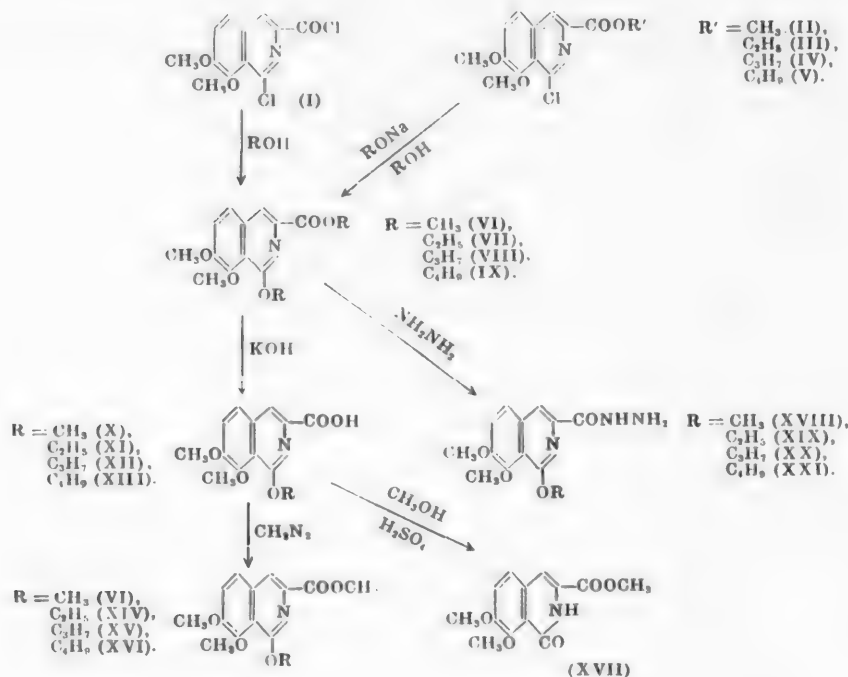
By the interaction, in the cold, of acid chloride (I) with methyl alcohol, we obtained, as previously reported, the methyl ester of 1,7,8-trimethoxy-3-isoquinolinecarboxylic acid [2]. It was of interest to establish

whether this is a general reaction; i.e.,whether esters of 1-alkoxy-substituted isoquinolinecarboxylic acids are formed by the interaction of this acid chloride with other alcohols. It was shown that the reaction of the chloro-substituted acid chloride (I) with ethyl, propyl, and butyl alcohols proceeds as in the case of methyl alcohol. In addition to the methyl ester of 1,7,8-trimethoxy-3-isoquinolinecarboxylic acid (VI), we obtained by means of this reaction the ethyl ester of 1-ethoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (VII), the propyl ester of 1-ethoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (VII), the propyl ester of 1-propoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (VIII), and the butyl ester of 1-butoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (IX). These same esters were obtained by heating the esters of 1-chloro-7,8-dimethoxy-3-isoquinolinecarboxylic acid with the equivalent amounts of the sodium alcoholates. It was found that simultaneously with the replacement of the chlorine by the alkoxy group, transesterification of the ester occurred, catalyzed by the metal alcoholate. Therefore the reaction resulted in the formation of an ester with the radical of that alcohol which served as the solvent during the reaction.

Alkaline hydrolysis of these esters of alkoxy-substituted acids (VI-IX) gave the four homologous acids differing in the alkoxy group in the 1-position of the isoquinoline ring: 1,7,8-trimethoxy-3-isoquinolinecarboxylic acid (X), 1-ethoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (XI), 1-propoxy-7,8-dimethoxy-3-isoquinoline-carboxylic acid (XII), and 1-butoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (XIII). The methyl esters (VI, XIV, XV, XVI) of these four acids were obtained by means of diazomethane.

In attempts to prepare the esters of these acids by heating these acids with the alcohols and sulfuric acid, it was found that, in addition to esterification of the carboxyl group, hydrolysis of the alkoxy group in the 1-position also occurred, and, as a consequence of this, there were obtained the esters of 7,8-dimethoxy-3-iso-carbostyrilcarboxylic acid and that alcohol which served as the reaction medium (XVII).

The increase in the mobility of the alkoxy group occurs in acid medium. In a neutral medium and also in an alkaline medium, as shown by the alkaline hydrolysis of the esters, this alkoxy group has considerable stability. The literature contains no indications of the lability of alkoxy groups connected to an isoquinoline nucleus; only for the pyridine and quinoline series are there facts known indicating a high mobility of alkoxy groups in α- and γ-positions to the nitrogen [3]. Just as in the case of the increased mobility of chlorine [2], the increased mobility, in acid medium, of the alkoxy group in the 1-position in the isoquinoline nucleus can apparently be explained on the basis that the nitrogen, adding a proton, acquires a positive charge which results in an increase in the shift of the electron cloud in the isoquinoline ring toward the nitrogen. Therefore, nucleophilic substitution in the isoquinoline ring proceeds readily, especially in the 1-position which is, of course, alpha to the nitrogen. Electronegative substituents meta to the alkoxy group apparently have an effect on its mobility.

The effect of the nitrogen on the ease of replacement of the methoxy by a hydroxyl group apparently extends to other positions of the isoquinoline ring also. This is supported by the hydrolysis of an alkoxy group in the 7- or 8-position in 7,8-dimethoxy-3-isocarbostyrilcarboxylic acid when this compound is heated with butyl alcohol and sulfuric acid on a boiling water bath, as we reported previously [1].

Esters (VI-IX) were used for the preparation of the hydrazides of the acids. The hydrazides of 1,7,8-tri-methoxy-3-isoquinolinecarboxylic acid (XVIII), 1-ethoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (XIX), 1-propoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (XX), and 1-butoxy-7,8-dimethoxy-3-isoquinoline-carboxylic acid (XXI) were prepared.

The resulting hydrazides (XVIII-XXI) were tested for chemotherapeutic activity by the Division of Chemotherapy of the All-Union Chemical-Pharmaceutical Scientific Research Institute. The tests showed that none of these preparations are active with respect to tuberculosis culture. This confirms the high specificity of the action of the hydrazides of isonicotinic acid, especially of phthivazide.

These esters of alkoxy-substituted acids of the isoquinoline series can be used for the preparation of other derivatives of acids of the isoquinoline series (amides, etc.), the synthesis of which is of interest in connection with the possible development of physiological activity in these groups of compounds.

EXPERIMENTAL

Preparation of esters of 1-alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acids. a) Alcoholysis of the

chloride of 1-chloro-7,8-dimethoxy-3-isoquinolinecarboxylic acid. A mixture of 2.86 g of the chloride of 1-chloro-7,8-dimethoxy-3-isoquinolinecarboxylic acid (I) and 10 ml of absolute alcohol (methyl, ethyl, propyl, or butyl) was allowed to stand for 16 hours in a closed flask at room temperature. Slow solution of the solid material occurred.

For the separation and purification of the methyl ester of 1,7,8-trimethoxy-3-isoquinolinecarboxylic acid (VI), the ethyl ester of 1-ethoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (VII), and the propyl ester of 1-propoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (VIII), the solution was poured into 200 g of an ice-water mixture containing 1.5 g of Na_2CO_3. The precipitated crystals were filtered, washed with water to a neutral reaction toward phenolphthalein, and recrystallized from the alcohols.

The butyl ester of 1-butoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (IX) was separated by washing the reaction mixture with water, a solution of sodium carbonate, and again with water to a neutral reaction toward phenolphthalein. The solution of the product in butyl alcohol was dried with sodium sulfate, the butyl alcohol was distilled under vacuum, and the ester was recrystallized from petroleum ether by cooling.

b) The action of sodium alcoholates on the corresponding esters of 1-chloro-7,8-dimethoxy-3-isoquinoline-carboxylic acid. The methyl ester of 1,7,8-trimethoxy-3-isoquinolinecarboxylic acid (VI) was prepared as follows. A solution of 0.23 g of sodium in 40 ml of absolute methyl alcohol was added to a mixture of 2.81 g of the methyl ester of 1-chloro-7,8-dimethoxy-3-isoquinolinecarboxylic acid. The reaction mixture was heated in a flask on a boiling water bath for 8 hours; the flask was provided with a reflux condenser which opened to the atmosphere through a calcium chloride tube. The resulting solution was cooled and poured into 320 g of a water-ice mixture. The precipitated crystals of the ester were filtered, washed with water to a neutral reaction toward phenolphthalein, and recrystallized from methyl alcohol. An organic acid (0.26 g) was obtained by acidification of the filtrate remaining after separation of the ester which crystallized when the reaction mixture was decanted on the ice.

In a similar manner were prepared the ester (VII) from the ethyl ester of 1-chloro-7,8-dimethoxy-3-iso-quinolinecarboxylic acid (III) (2.96 g), ester (VIII) from the propyl ester of 1-chloro-7,8-dimethoxy-3-iso-quinolinecarboxylic acid (IV) (3.1 g), and ester (IX) from the butyl ester of 1-chloro-7,8-dimethoxy-3-iso-quinoline-carboxylic acid (V) (3.24 g). Esters (VII) and (VIII) were recrystallized from the alcohols. In the preparation of the butyl ester (IX), only 3.5 ml of butyl alcohol was in the reaction mixture, and for the separation of the ester, the reaction mixture was diluted with 50 ml of dioxane; the resulting solution was decanted into 500 g of a mixture of water and ice, and the precipitated ester was filtered, washed with water to a neutral reaction toward phenolphthalein, and recrystallized from ethyl ether and petroleum ether by cooling.

c) The action of sodium alcoholates on the methyl ester of 1-chloro-7,8-dimethoxy-3-isoquinoline-carboxylic acid (during transesterification). To a solution of 2.81 g of the methyl ester of 1-chloro-7,8-di-methoxy-3-isoquinolinecarboxylic acid (II) in 40 ml of absolute alcohol (ethyl, propyl, or butyl) was added a solution of 0.23 g of sodium in 40 ml of the same alcohol. The mixture was heated for 16 hours on a boiling water bath; the reaction vessel comprised a flask fitted with a reflux condenser connected to a calcium chloride tube. Separation of the esters from the reaction mixtures was carried out as in Experiment "b". The esters (VII)-(IX) were prepared in this manner.

The melting points of the corresponding esters prepared in Experiments "a", "b", and "c" were in agreement. Mixed samples of the corresponding esters prepared by the different methods showed no depression of the melting point. The melting points, yields, and analytical date for the substances prepared are presented in the table.

These esters of 1-alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acids (VI)-(IX) are crystalline substances; the melting points of the higher homologs are lower than those of the lower homologs. The esters distill under vacuum without decomposition. The substances are readily soluble in organic solvents and practically insoluble in water. The salts of these esters separate when dry hydrogen chloride is passed into solutions of these esters in ethyl ether; these salts are hydrolyzed by water.
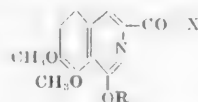
Preparation of 1-alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acids. 1,7,8-Trimethoxy-3-isoquinoline-carboxylic acid (X) was prepared by heating for 30 minutes the methyl ester of 1,7,8-trimethoxy-3-isoquinoline-carboxylic acid (VI) (2.77 g) with 20 ml of 10% sodium hydroxide solution. The solution was filtered, and

the filtrate was acidified with 10% hydrochloric acid (until acid toward Congo indicator). The precipitated acid was filtered, washed with water, and recrystallized from methyl alcohol. In a similar manner were prepared 1-ethoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (XI) from ester (VII) (3.1 g), 1-propoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (XII) from ester (VIII) (3.3 g), and 1-butoxy-7,8-dimethoxy-3-isoquinoline-carboxylic acid (XIII) from ester (IX) (3.6 g).

These 1-alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acids (X)-(XIII) are crystalline materials; the melting points of the higher homologs are lower than those of the lower homologs. The acids are difficultly soluble in water and readily soluble in the majority of organic solvents, and the solubility increases with an increase in the molecular weight of the acid. They may be crystallized from alcohols.

Preparation of the methyl esters of 1-alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (by the action of diazomethane on the corresponding acids). 10 ml of an ether solution of diazomethane was added to a solution of 0.1 g of the 1-alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (X)-(XIII) in 10 ml of methyl alcohol. The excess diazomethane and the solvent were distilled. The residue was dissolved in 5 ml of methyl alcohol, and the solution was filtered and poured into 20 g of a mixture of water and ice containing 0.25 ml of 10% sodium carbonate solution. The precipitated ester was filtered, washed with water to a neutral reaction toward phenolphthalein, and recrystallized from methyl alcohol. The methyl esters of 1,7,8-trimethoxy-3-iso-quinolinecarboxylic acid, 1-ethoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid, 1-propoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid, and 1-butoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (VI), (XIV), (XV), (XVI) were prepared. The esters are crystalline substances; the melting points of the higher homologs are lower than those of the lower homologs. They are practically insoluble in water and are readily soluble in the majority of organic solvents.

1-Alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic Acids and Their Derivatives

Compound No.	R	X	Melting point	Formula	Elemental composition (in %)						Yield (in %)
					Found			Calculated			
					C	H	N	C	H	N	
VI	CH_3	OCH_3	131°	$C_{14}H_{15}O_5N$	60.68	5.34	4.95	60.64	5.45	5.05	85 *, 81 **
VII	C_2H_5	OC_2H_5	86	$C_{16}H_{19}O_5N$	62.91	6.35	4.54	62.94	6.27	4.59	97 *, 75 **
VIII	C_3H_7	OC_3H_7	69—70	$C_{18}H_{23}O_5N$	64.86	6.88	4.25	64.86	6.95	4.2	65 *, 80 **
IX	C_4H_9	OC_4H_9	51—52	$C_{20}H_{27}O_5N$	66.33	6.63	3.83	66.46	7.53	3.88	36 *, 63 **
X	CH_3	OH	185	$C_{13}H_{13}O_5N$	59.25	5.01	5.38	59.32	4.98	5.32	97
XI	C_2H_5	OH	153	$C_{14}H_{15}O_5N$	60.60	5.53	5.02	60.64	5.45	5.05	96
XII	C_3H_7	OH	136	$C_{15}H_{17}O_5N$	61.86	5.93	4.85	61.84	5.88	4.81	89
XIII	C_4H_9	OH	127	$C_{16}H_{19}O_5N$	63.04	6.22	4.68	62.94	6.27	4.59	87
XIV	C_2H_5	OCH_3	114	$C_{15}H_{17}O_5N$	61.88	5.88	4.90	61.84	5.88	4.81	97
XV	C_3H_7	OCH_3	86	$C_{16}H_{19}O_5N$	62.92	6.27	4.56	62.94	6.27	4.59	95
XVI	C_4H_9	OCH_3	85	$C_{17}H_{21}O_5N$	63.99	6.67	4.33	63.93	6.63	4.39	87
XVIII	CH_3	$NHNH_2$	196—197 (with decomp.)	$C_{13}H_{15}O_4N_3$	56.12	5.43	15.31	56.36	5.42	15.16	93
XIX	C_2H_5	$NHNH_2$	196—197 (with decomp.)	$C_{14}H_{17}O_4N_3$	—	—	14.46	—	—	14.43	95
XX	C_3H_7	$NHNH_2$	169—172	$C_{15}H_{19}O_4N_3$	—	—	13.74	—	—	13.76	92
XXI	C_4H_9	$NHNH_2$	169—170	$C_{16}H_{21}O_4N_3$	—	—	13.38	—	—	13.16	94

Notes. * — in Experiment "a"; ** — in Experiments "b" and "c".

Acid hydrolysis of the alkoxy group in the 1-position of 1-alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acids. A mixture of 0.26 g of 1,7,8-trimethoxy-3-isoquinolinecarboxylic acid (or 0.31 g of 1-butoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid), 5 ml of methyl alcohol, and 0.15 ml of sulfuric acid (d 1.84) was placed

in a flask fitted with a reflux condenser, which was connected to a calcium chloride tube, and the mixture was heated on a boiling water bath for 6 hours. The resulting solution was poured into 15 g of ice and water containing 0.3 g of sodium carbonate. The crystallized ester was filtered and washed with water to a neutral reaction toward phenolphthalein. The yield was 0.17 g (65 %) of the methyl ester of 7,8-dimethoxy-3-isocarboxystyril-carboxylic acid, m.p. 195° (from methyl alcohol). According to the literature, the m.p. is 195° [1,4]. When a mixed sample with the methyl ester of 7,8-dimethoxy-3-isocarbostyrilcarboxylic acid prepared by us previously [1] was melted, no depression of the melting point was observed.

Preparation of the hydrazides of 1-alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acids. For the preparation of the hydrazide of 1,7,8-trimethoxy-3-isoquinolinecarboxylic acid (XVIII), a solution of 0.55 g of the methyl ester of 1,7,8-trimethoxy-3-isoquinolinecarboxylic acid (VI) in 20 ml of ethyl alcohol was poured into 5 ml of 85% hydrazine hydrate. Crystals of the hydrazide appeared after 10-15 minutes. The reaction mixture was allowed to stand overnight at room temperature, after which the crystalline product was filtered and washed with alcohol. The hydrazide was recrystallized from ethyl alcohol. In a similar manner were prepared the hydrazide of 1-ethoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (XIX) from ester (VII) (0.61 g), the hydrazide of 1-propoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (XX) from ester (VIII) (0.67 g), and the hydrazide of 1-butoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acid (XXI) from ester (IX) (0.72 g). The hydrazides were recrystallized from alcohol.

SUMMARY

1. A series of homologous trialkoxy-substituted acids of the isoquinoline series differing in the alkoxy group at the 1-position of the isoquinoline nucleus were prepared.

2. A series of esters and hydrazides of these acids were prepared.

3. It was shown that in 1-alkoxy-7,8-dimethoxy-3-isoquinolinecarboxylic acids, the alkoxy group in the 1-position of the isoquinoline nucleus is mobile in acid medium and is readily hydrolyzed.

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• •In Russian.

REGULARITIES IN THE CHANGES IN ACIDITY AND BASICITY IN HOMOLOGOUS SERIES OF α,ω-DIFUNCTIONAL COMPOUNDS

I. REGULARITIES IN THE CHANGES IN ACIDITY IN HOMOLOGOUS SERIES OF ω-HALO-SUBSTITUTED ALIPHATIC n-CARBOXYLIC ACIDS

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As is well known, the reason for the increased acidity of polar-substituted aliphatic carboxylic acids and the increased reactivity of the substituent itself is a mutual effect of an electrostatic nature. The substituting atom (or group of atoms), owing to its electronegativity (halogens), its weakly shielded positive charge ($\overset{+}{N}H_3$), or its dipole structure (CN, NO_2). causes a successive shift of the electron density in its own direction (inductive shift") along the line of σ-bonds or else acts directly through space. In one way or another, in the resulting field, the protonized hydrogen atom of the COOH group exhibits in the field a more or less highly positive potential which decreases the work required for its ionization.

In conformity with the different routes by which the mutual effect is accomplished, it is customary to distinguish an inductive effect , which is transmitted through the chain of atoms along the line of covalent bonds, and an electrostatic effect of the field, which operates through space - through the solvent [1]. Up to the present. these two effects have not been separated in practice. The changes in acidity resulting from a polar substitutent can be qualitatively explained by each of these effects; a theoretical and semiquantitative interpretation of these changes presently exists only for the field effect. Therefore, the inductive effect, the nature of which is not clear, is sometimes considered as a special case of the field effect [2].
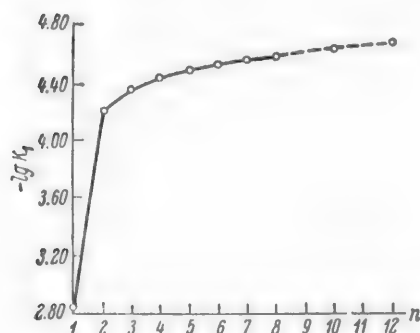
Fig. 1. Dependence of the index of the degree of dissociation ($pK_1 = -\log K_1$) of aliphatic n-α,ω-dicarboxylic acids of the general formula $HOOC(CH_2)_n COOH$ on the length of the carbon chain (n).

The quantitative interpretation of the over-all electrostatic factor and its effect on the strength and reactivitiy of polar-substituted acids finds confirmation from two different directions. There are the simple, but completely empirical, methods of calculation [3-5], the best known of which is the equation of Hammett [5]. On the other hand, the change in acid strength can be calculated, in a number of cases, using the concepts of the classical electrostatic field, for example, by means of the equations of Bjerrum [6, 7], Ingold [8], and Kirkwood and Westheimer [9, 10]. The inaccuracy of these methods is, in our opinion, due not only to the difficulties in taking into consideration a series of complex factors [11, 12], but also partially to the one-sided nature of the basic concept.

A characteristic feature of the electrostatic effect is its rapid attenuation with distance between the atoms or groups mutually affecting each other. Thus, for example, as is well known, the acidity of ω-substituted ali-

phatic n-carboxylic acids rapidly decreases with the length of the carbon chain (Figure 1).

It seemed to us to be of interest to study the electrostatic effect from the point of view of its attenuation; i. e., 1) to determine the dependence of the index of dissociation, $pK_n = -lgK_n$, of acids having the general formula $X(CH_2)_nCOOH$ on the length of the carbon chain, as indicated by $\underline{n}$, and to develop an equation for pK_n as a function of $\underline{n}$; 2) to determine whether this functional relationship is general for all ω-polar-substituted n-carboxylic acids; and 3) to establish regular relationship between the parameters in the equation relating pK_n to $\underline{n}$ and the physical values characterizing the substituent X.
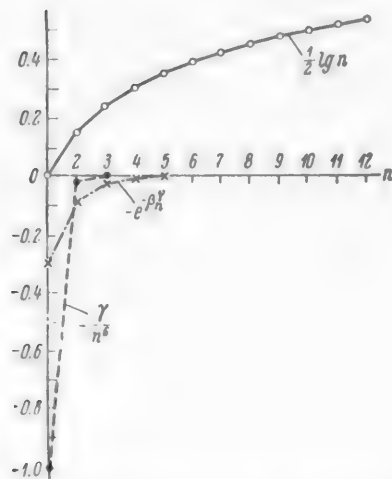
Fig. 2. Dependence of the changes in the terms of Equation (1) on the length of the carbon chain (n) for aliphatic n-α,ω-di-carboxylic acids.

As we have established, the indices of dissociation for X = Cl, Br, I, COOH, and, evidently, also for F, CN, OH, and SH increase with an increase in $\underline{n}$ according to the same law:

$$pK_n = -\frac{\gamma}{n^\delta} - e^{-\beta n^\varphi} + \frac{1}{2} \lg n + \delta, \qquad (1)$$

where: γ, δ, φ and β are constants for a given substituent (Table 1).

In Figure 2 is shown the change in the terms of Equation (1) with n, which expresses the length of the carbon chain, for α,ω-dicarboxylic acids.

The first term of Equation (1) is effective only for $n < 2$; the second term is effective to $n \leq 3$. For $n \geq 4$, Equation (1) assumes a very simple form, namely:

$$pK_n = \frac{1}{2} \lg n + \delta. \qquad (2)$$

Equation (2) is very accurate; for example, it permits calculation of values of pH for α,ω-dicarboxylic acids with deviations from the experimental values not exceeding $\pm$ 0.01 (Table 2). In Table 3 are presented the indices of acidity of ω-monohalo-substituted aliphatic n-carboxylic acids calculated by means of Equation (1).

The physical significance of the individual terms of Equation (1) are apparent in the group of ω-halocarboxylic acids. The constants γ and δ for this group, at least for Cl, Br, and I, are ideally linear functions of the electron affinity and polarizability of the halogen or of the dipole moment of the halogen-carbon bond:

$$\gamma = 0.55E - 1.37, \qquad (3)$$

$$\gamma = 0.96 - 0.044R, \qquad (4)$$

$$\gamma = 1.2\mu - 1.10, \qquad (5)$$

where: E is the electron affinity of the halogen in ev (from reference [17], R is the atomic refraction of the halogen in cm^3 g-atom^{-1}) (from reference [18]), and μ is the dipole moment of the halogen-carbon bond (in D) (from reference [19]) (Figures 3 and 4).

The values of δ for the halogens can be calculated from similar equations (See Figure 5):

$$\delta = 4.93 - 0.14E, \qquad (6)$$

$$\delta = 11.35 \cdot 10^{-3} R + 4.33, \qquad (7)$$

$$\delta = 4.85 - 0.3\mu. \qquad (8)$$

TABLE 1

Values of the Constants of Equation (1) for Some Substituents X

X	δ	γ	β	φ
Cl	4.40	0.70	0.20	2
Br	4.43	0.57	0.032	4
I	4.49	0.35	0.030	4
COOH	4.13	1.00	1.20	1

TABLE 2

Indices of the First Stage of Dissociation of Aliphatic n-Dicarboxylic Acids, $HOOC(CH_2)_n COOH$, Calculated by Means of Equations (1) and (2).

n	pK	
	Calculated	Experimental (25°)*
1	2.83	2.83
2	4.17	4.19
3	4.34	4.34
4	4.42	4.42
5	4.48	4.48
6	4.52	4.52
7	4.55	4.55
8	4.58	4.61
10	4.63	4.64
12	4.67	4.67

The ratio of the dissociation constants K_1 and K_2 for members of the homologous series $X(CH_2)_n COOH$ (X=Cl,Br,I) is also a linear function of E, R, or μ (Figure 6):

$$\frac{K_1}{K_2} = 13.4E - 34.4, \qquad (9)$$

$$\frac{K_1}{K_2} = 22.4 - 1.072R, \qquad (10)$$

$$\frac{K_1}{K_2} = 29\mu - 27.5. \qquad (11)$$

Values of γ, δ, and K_1/K_2 for fluorine calculated from E and from R are in agreement ($\gamma=0.90$, $\delta=4.35$), but they differ from the values calculated from μ, which are equal to the corresponding values for bromine (since the dipole moments for the $C-Br$ and $C-F$ bonds are equivalent [19]). The linear dependence does not in all cases extend to fluorine; thus, for example, the potential of the electrostatic field calculated for the monohaloacetic acids [16], but only in the case of Cl, Br, and I, depend linearly on the electron affinity of the halogen. The true value of δ for F could be calculated, using Equation (2), from the dissociation constants of δ-fluorovaleric acid or ϵ-fluorocaproic acid, but the strength of these acids, as is the case for all members of the series X=F with n> 1, is presently unknown.

The constants β and φ do not usually vary from chlorine to iodine.** The majority of the physical constants of halogen atoms and ions, as well as the thermodynamic functions of halogen-substituted compounds, are about the same for chlorine and bromine, and vary more or less sharply for fluorine and iodine, attaining a maximum or minimum. The dipole moments of halogen-carbon bonds (maximum for Cl),*** the mobility of the ions (maximum for Br⁻), and the change in heat content and heat capacity during ionization of monohaloacetic acids (extreme value for Cl [16]) are all exceptions. It must be assumed that the extremes of physical constants for Cl or Br are due to the convergence of two or more inversely varying effects, for example, electron affinity and polarizability.

The regularities in the change of acidity in the ω-halo-substituted aliphatic n-carboxylic acids, in spite of their empirical nature, shed some light on the role of the individual factors determining the intensity of the electrostatic mutual effect.

Equation (1) can be written in the form:

$$\Delta G = -2.303RT \lg K_n = A = A_1 + A_2 + A_3 \qquad (1\text{-}a)$$

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* Data for members of the series up to n = 7 were taken from reference [13], for n=8, 10, and 12 from reference [14], taking into account that the values of pK for the first stage of dissociation of aliphatic dicarboxylic acids in 20% aqueous methanol average 0.43 greater than the values of pK in water, reported in reference [13].
** The values of δ for Br and I, in all probability, are not quite the same, but any attempt to increase their precision seems unwarranted to us, owing to the errors in the experimental values of the dissociation constants.
*** It is interesting that the portion of p-electrons in the electron cloud of halogen atoms vary from fluorine to iodine directly with the dipole moment of the halogen-carbon bond.

where: ΔG is the change in the change in free energy (more precisely, free enthalpy) of the dissociation reaction; A is the maximum (useful) work of dissociation; A_1, A_2, A_3 are the components of this work, and are equal, respectively, to $RT \cdot \gamma / n^6$, $-2.303 RTe^{-\beta n \cdot \varphi}$, $2.303 RT \lg \Delta \sqrt{n}$, where $\lg \Delta = \delta$. The term A_1 disappears completely for $n \geq 2$; we assume, therefore, that it represents the energy associated with the inductive moment; this energy, in the case of a pole (single charge), is inversely proportional to the 4th power of the distance, and in the case of a dipole it is inversely proportional to the 6th power of the distance [20]. The distance law and the direct dependence on the polarizability of the halogen, which characterizes the deformability of the electron cloud and the strength of the coupling of the electrons dispersed in an electric field, in our opinion indicates the presence of an inductive polarization effect.

TABLE 3

Indices of Acidity of ω-Monohalo-Substituted n-Carboxylic Acids
$X(CH_2)_n COOH$ Calculated by Means of Equation (1)

Nos.	X	n	pK	
			Calculated	Experimental (25°) *
1		1	2.88	2.87
2		2	4.09	4.07
3	Cl	3	4.47	4.52
4		4	4.66	4.69
5		5	4.74	4.75
6		6	4.79	4.79
7		1	2.89	2.90
8	Br	2	3.97	4.01
9		3	4.59	4.59
10		4	4.73	4.72
11		1	3.17	3.175
12	I	2	4.02	4.05
13		3	4.64	4.64
14		4	4.79	4.77

* Data for the members of all series with $n > 1$ were taken from reference [15]. The data for the monohaloacetic acids are new precise data obtained conductometrically [16].
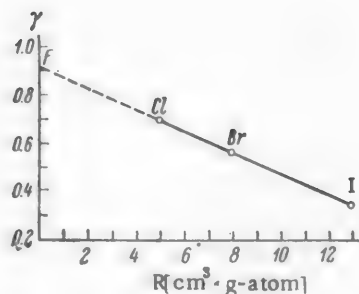
Fig. 3. Dependence of γ for ω-halo-substituted aliphatic n-carboxylic acids on the atomic refraction (R) of the halogen.
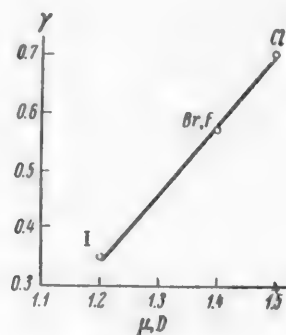
Fig. 4. Dependence of γ for ω-halo-substituted aliphatic n-carboxylic acids on the dipole moment (μ) of the halogen-carbon bond.
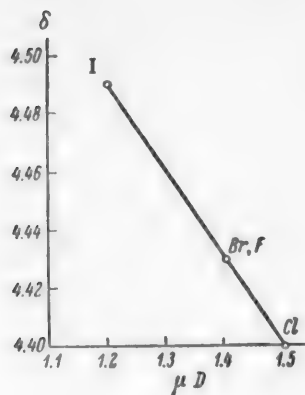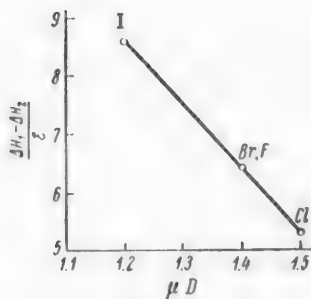
Fig. 5. Dependence of the constant δ for ω-halo-substituted aliphatic n-carboxylic acids on the dipole moment (μ) of the halogen-carbon bond.
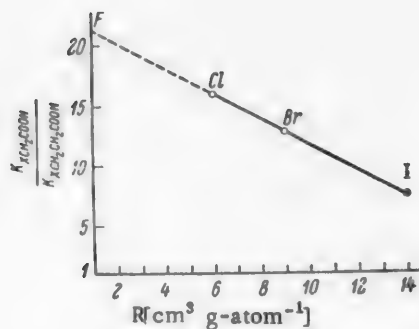

Fig. 6. Dependence of the ratio of the first and second dissociation constants for members of the homologous series $X(CH_2)_n COOH$ ($X = Cl, Br, I$) on the atomic refraction (R) of the halogen.

Fig. 7. Dependence of the ratio $(\Delta H_1 - \Delta H_2)/\delta$ of the carbon-halogen bond.

A_3 evidently represents the work associated with the electric field created by the substituent atom or group of atoms and the polarized hydrogen atom of the COOH group, which is polarized through the solvent. The manner in which A_1 and A_3 depend on the dielectric constant (D) of the solvent must therefore be different; A_3 must be inversely proportional to D, while A_1 is independent of D. The difficulty of taking into account the "true", effective dielectric constant in the Kirkwood-Westheimer model is, in our opinion, due not so much to complications of the calculation [11] as to ignoring of the inductive method of transference of the mutual effect.

When the distance between the groups mutually affecting each other is of the order of $4CH_2$, the only route by which the mutual effect is transferred becomes the field— the solvent; in our opinion, bending of the polymethylene chain must contribute to this mechanism. *

All energy values of an electrostatic nature must enter into the enthalpy change of the dissociation reaction, i. e., into the first term, ΔH^0, of the equation for the free energy of the reaction.

$$\Delta G^0 = \Delta H^0 + \int_0^T \Delta C_p dT - T \int_0^T \frac{\Delta C_p}{T} dT - T \Delta S^0$$

Among the monohaloacetic acids, the ratio $(\Delta H_1 - \Delta H_2)/\delta$ (ΔH_1, ΔH_2 are the changes in heat content of the unsubstituted and substituted acids, δ is the field potential) is a minimum for chloroacetic acid [16],

* In solutions of filiform molecules, molecules with sufficiently long polymethylene chains (n> 4), the statistical weight of the spherical structure (constellations) increases with an increase in chain length. The most probable average distance L between the ends of such a long chain, which consists of N links (C—C) which rotate about each other, is proportional to $\sqrt{N}$ or $\sqrt{n+1}$; as shown above, $-\lg K_n$ is proportional to $\lg\sqrt{n}$, i. e., to $\sqrt{L^2-1}$.

while δ, as we have shown, increases linearly with the electron affinity of the halogen from iodine to chlorine and then, at a slower rate, to fluorine. It can be shown that the ratio $(\Delta H_1 - \Delta H_2)/\delta$ depends linearly on the dipole moment of the C–X bond (Figure 7):

$$\frac{\Delta H_1 - \Delta H_2}{\delta} = a - b\mu, \tag{12}$$

where $\underline{a}$ and $\underline{b}$ are constants for each group of halogens.
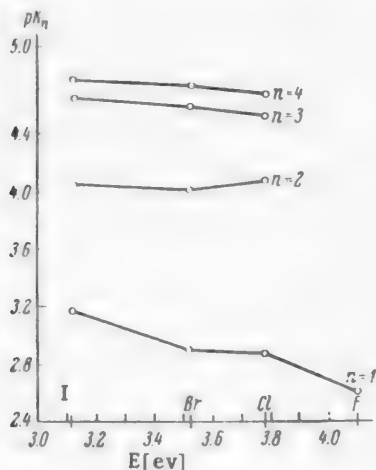
Fig. 8. Dependence of the index of ω-halo-substituted aliphatic n-carboxylic acids on the electron affinity (E) of the halogen.
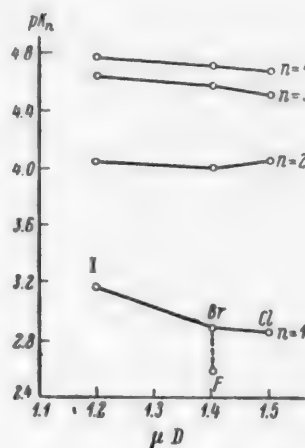
Fig. 9. Dependence of the index of dissociation of ω-halo-substituted aliphatic n-carboxylic acids on the dipole moment (μ) of the halogen-carbon bond.

It is impossible to explain the increase in dissociation of acetic acid, due to substitution of halogen, by the field effect alone. The nature of the changes in ΔH and ΔC_p for monohaloacetic acids (minimum for Cl [16]) also supports the contention of a complex electrostatic effect. Evidently, both components of this effect increase the acidity; one increases from I to F (field effect, uniformly increasing with electron affinity), and the other increases (polarizability) from F to I.

The existence of different mechanisms for the transfer of the electrostatic effect at small distances can be conjectured from Figures 8 and 9; the dependence of pK_n on the electron affinity of the halogen and the dipole moment of the C–X bond differs for n=1, 2 and 3, and levels out only for n = 3 and 4.

The physical significance of the term A_2 of the equation (1-a) still remains obscure. The attenuation law of this term indicates a connection with A_1. To a certain approximation

$$\frac{E}{\gamma + e^{-\rho}} = \text{const} = 2.38 \pm 0.10. \tag{13}$$

Moreover, that A_2 reflects some of the change in entropy and heat capacity accompanying the dissociation of the acids and is connected with peculiarities of the solvation of the undissociated acids and their ions by the solvent cannot be ignored.

SUMMARY

1. An empirical equation was developed expressing pK_n as a function of $\underline{n}$ for the homologous series of ω-polar-substituted aliphatic n-carboxylic acids $X(CH_2)_n COOH$ (X=Cl, Br, I, COOH).

2. The regularities of the dependence of the constants of this equation on the electron affinity and atomic refraction (polarizability) of the halogen and on the dipole moment of the halogen-carbon bond were established for a group of ω-monohalo-substituted aliphatic n-carboxylic acids.

3. These regularities and the nature of the changes in certain thermodynamic functions of the dissociation reaction indicate the complex nature of the electrostatic effect.

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*Russian translation.

ACYLAMINO DERIVATIVES OF NUCLEOSIDES

III. SYNTHESIS OF ACYLAMIDO DERIVATIVES OF ADENOSINE AND 9-β-D-GLU-COPYRANOSYLGUANINE

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In previously published papers [1, 2], we described a method for the synthesis of acylamido and peptide derivatives of nucleosides in which the amino group [3] of the latter is bonded through an amide bond with α-amino acids as well as with di - and tripeptides. The aim of the present work was the development of a method of synthesis of acylamido derivatives of purine aminonucleosides, which form part of the composition of nucleic acids - adenosine and guanosine.

The initial adenosine was separated from adenosinetriphosphoric acid (ATP); in carrying out the separation, we also found conditions for the hydrolysis of ATP under which it was possible to direct the cleavage of the ATP in either of two directions:

Adenosine   Adenosine-5'-phosphoric acid
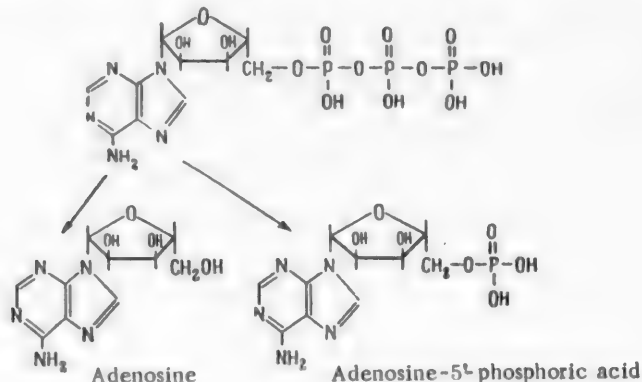
If the hydrolysis of ATP is carried out in a 50% aqueous solution of pyridine in an autoclave at 110° for a period of 100 hours, the main product of the hydrolysis is adenosine, and adenosine-5'-phosphoric acid is present in the hydrolysis product only in small amounts. When the hydrolysis of ATP is carried out with a 30% aqueous solution of pyridine for 6 hours at 100° (atmospheric pressure), the main product is adenosine-5'-phosphoric acid. The course of the hydrolysis was followed by means of paper chromatography in isoamyl alcohol-5% Na_2HPO_4 solution as the solvent [4].

The adenosine was separated from the hydrolysis product obtained by hydrolysis of ATP with a 50% solution of pyridine (110°, 100 hours) by passing the hydrolysis product through EDE-10 (OH form) resin after precipitation of the free phosphoric acid. The adenosine-5'-phosphoric acid was adsorbed by the resin, and the adenosine stayed in the filtrate; the adenosine was precipitated from a concentrated solution. In the preparation of adenosine-5'-phosphoric acid, the hydrolysis product obtained by hydrolysis of ATP with a 30% pyridine solution was passed through KU-2(H+ form) resin. The adenosine was adsorbed on the resin, and the acid stayed in the filtrate, from

which it was precipitated after concentration of the solution. In either case, the adenosine-5'phosphoric acid and the adenosine formed during the hydrolysis were eluted from the ion exchange resin with acid (1 N) or a solution of ammonia (10 %).

As the other purine nucleoside, we used the closest analog of guanosine — 9-β-D-glucopyranosylguanine, which was prepared synthetically. On the basis of the data of Davoll and Lowy [5], who accomplished the synthesis of this nucleoside from 2,6-diaminopurine, we were successful in obtaining 9-β-D-glucopyranosylguanine from guanine by means of the following transformations:
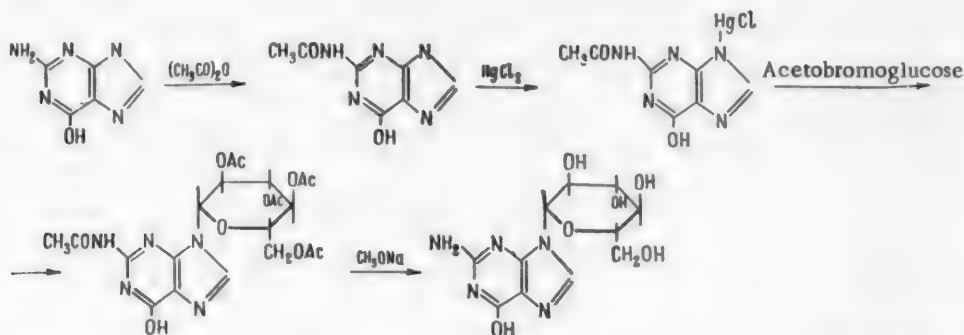
The resulting glucopyranosylguanine had a melting point and an R_f which were in agreement with the literature values [5]. However, a study of the u. v. absorption spectrum of this compound (λ_{max} 250 and 277 mμ) showed that it was a mixture of 9-β-D (λ_{max} 250 mμ) and 7-β-D-glucopyranosylguanine (λ_{max} 245 and 280 mμ) [6]. After repeated recrystallization from water, we were able to separate these two isomers. Only the 9-β-D-glucopyranosylguanine was introduced into the aminoacylation reaction.

The amino groups in adenosine and 9-β-D-glucopyranosylguanine are quite inert toward acylating agents. In contrast to cytosine nucleosides [1, 2], the amine groups in adenosine and guanosine are not acetylated in the cold by acetic anhydride [7]. Attempts to prepare acylamido derivatives of adenosine and 9-β-D-glucopyranosyl-guanine by acylation with mixed anhydrides, with cyanomethyl esters, and with thio esters of amino acids, as well as the use of the carbodiimide method, ended in failure. Aminoacylation (acylamidation) of these nucleosides could be carried out only with phthalylaminoacyl chlorides, for example:
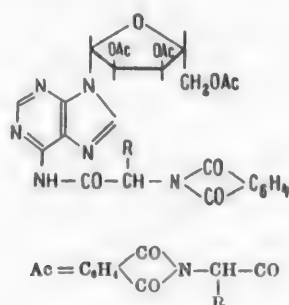

The reaction was carried out in absolute benzene in the presence of tributylamine or in absolute pyridine by refluxing for several hours. Under these conditions, triacetyladenosine was aminoacylated only at the amino group. Aminoacylation of free adenosine and of 9-β-D-glucopyranosylguanine occurred both at the amino group and at the hydroxyl groups of the sugar. Lists of the compounds synthesized are presented in Tables 1 and 2.

The acylamido derivatives of adenosine and 9-β-D-glucopyranosylguanine prepared by us were hygroscopic substances which lost water with difficulty when vacuum dried over P_2O_5. A study of the hydrolytic stability of the amide bond in these compounds showed that: a) long (up to 50 hours) refluxing did not hydrolyze the am-

ide bond; b) both the amide and the ester bonds are hydrolyzed by 30-minute refluxing with 0.1 N NaOH.

TABLE 1

N_6-Phthalylaminoacyl Derivatives of Adenosine
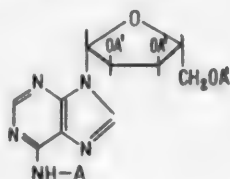
Compound No.	A	A'	Yield (%)	Constants		
				Melting point (with decomp)	λ max. in 96% alcohol ($m\mu$)	R_f *
(I)	Phthalylglycyl	Acetyl	51	118—120°	266—268	0.81
(II)	Phthalylglycyl	Phthalylglycyl	60	230	260—262	—
(III)	Phthalylglycyl	Acetyl	55	95—100	266	0.74
(IV)	Phthalylphenylalanyl	Acetyl	50	105—109	266	0.85

* Ascending chromatogram in n-butanol saturated with water, No. 2 chromatographic paper from the Leningrad plant.

TABLE 2

N_2-Phthalylaminoacyl Derivatives of 9-β-D-Glucopyranosylguanine
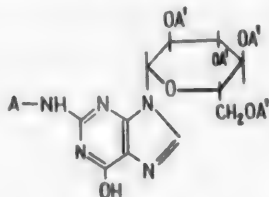
Compound No.	A	A'	Yield (in %)	Melting point (with decomp.)
(V)	Phthalylglycyl	Phthalylglycyl	78	150—155°
(VI)	Phthalylglycyl	Phthalylvalyl	65	123—125
(VII)	Phthalylphenyl-alanyl		40	160—165

In the examples studied by us, no sharp difference was detected in the nature of the amide bond in acyl-amido derivatives of adenosine and guanine nucleosides.

EXPERIMENTAL

Separation of adenosine. A solution of 10 g of ATP in 150 ml of a 50% aqueous solution of pyridine was heated in an autoclave at 110° for 100 hours. The solution was evaporated to dryness under vacuum, the sirup

was dissolved in 50 ml of water, and a saturated solution of $Ba(OH)_2$ was added to the solution until it was weakly alkaline. The precipitated $Ba_3(PO_4)_2$ was filtered and washed with hot water. The filtrate and wash water were evaporated under vacuum to 20 ml, and acidified with concentrated H_2SO_4 to a weakly acid reaction; the $BaSO_4$ was filtered and the filtrate was passed through ÉDÉ-10 (OH⁻ form) resin (1.5 × 30 cm). The column was washed with water (200 ml), and the filtrate and wash water were evaporated under vacuum to 50 ml. A voluminous precipitate (needle clusters) formed in the cooled solution, and this was filtered and recrystallized from water. After the material was dried at 100°, the m. p. was 235°. The literature value for the m. p. is 234-235° [8]. The yield was 4.2 g. Absorption in the u. v. (96% C_2H_5OH): λ_{max} 260 mμ (ϵ 1700), Rf 0.55 (isoamyl alcohol - 5% solution of Na_2HPO_4).

Separation of adenosine-5'-phosphoric acid. A solution of 5 g of ATP in 150 ml of a 30% aqueous solution of pyridine was refluxed for 6 hours, and evaporated under vacuum—the residue was dissolved in 10 ml of water. A saturated solution of $Ba(OH)_2$ was added to the solution to a weakly alkaline reaction. The precipitated $Ba_3(PO_4)_2$ was filtered and washed with hot water. The filtrate and wash water were evaporated to 20 ml. The solution was chromatographed •with isoamyl alcohol—5%solution of Na_2HPO_4 as the solvent. On the descending chromatogram were observed two spots with Rf of 0.55 and 0.70, which correspond to adenosine and adenosine-5'-phosphoric acid. the adenosine spot being considerably smaller. The solution was passed through KU-2 resin (H⁺ form) (1 × 20 cm). The column was washed with water (150 ml); the filtrate and wash water were evaporated under vacuum to 50 ml. A precipitate formed in the cooled solution, and this was filtered and washed with water. The adenosine-5'-phosphoric acid was recrystallized from water and dried at 100°. M. p. 200° (with decomposition). The literature value for the m. p. is 196-200°. The yield was 2.3 g. Absorption in the u. v. (96% C_2H_5OH): λ_{max} 260 mμ (ϵ 14 500).

Preparation of the acetyl derivatives of adenosine. Triacetyladenosine was prepared by the method of reference [7]. M. p. 170°, Rf 0.70 (isoamyl alcohol-5% solution of Na_2HPO_4). Absorption in the u. v. (96% C_2H_5OH): λ_{max} 260 mμ (ϵ 9925).

Tetraacetyladenosine was also prepared by the method of reference [7]. The tetraacetyladenosine, which was obtained in the form of a syrup, was dissolved in benzene, and the solution was evaporated to dryness. After 3-fold evaporation of benzene solutions, the resulting material decomposed at 60-65°. Absorption in the u. v. (96% C_2H_5OH): λ_{max} 272 mμ (ϵ 8000). Rf 0.45 (ascending chromatogram in n-butyl alcohol saturated with water).

N_6-Phthalylglycyltriacetyladenosine (I). 0.2 ml of tributylamine was added to a solution of 0.3 g of triacetyladenosine and 0.2 g of phthalylglycyl chloride in 25 ml of absolute benzene. The solution was refluxed for 6 hours, cooled, and evaporated to dryness under vacuum. The oil was dissolved in 10 ml of alcohol, and 20 ml of water was added to the solution. The precipitate, which formed in the cooled solution, was filtered, washed with water, and reprecipitated once from alcohol (animal charcoal). The substance was dried in a vacuum desiccator over P_2O_5. Before analysis, the substance was dried under vacuum over P_2O_5 at 75° for 10 hours.

Found %: N 13.47. $C_{26}H_{24}O_{10}N_6 \cdot 2H_2O$. Calculated %: N 13.63.

N_6-Phthalylphenylalanyltriacetyladenosine (IV). A solution of 0.1 g of triacetyladenosine and 0.08 g of phthalylphenylalanyl chloride in 10 ml of pyridine was allowed to stand for 24 hours at 37°. The solvent was evaporated under vacuum, and the residue was dissolved in chloroform; the solution was washed with water, $NaHCO_3$ (10%). 1 N H_2SO_4, and again with water, and was dried over Na_2SO_4. Petroleum ether was added to the dried solution. The resulting precipitate was reprecipitated from chloroform. Before analysis, the material was dried under vacuum over P_2O_5 at 75° for two weeks.

Found %: C 59.31; H 4.65; N 12.41. $C_{33}H_{30}O_{10}N_6$. Calculated %: C 59.1; H 4.49 N 12.54.

Hydrolysis of (IV). The substance was heated with water for 50 hours. The u. v. absorption characteristic of the amino group in phthalylaminoacyl derivatives of adenosine (λ_{max} 268 mμ) was unchanged.

0.01 g of (IV) was heated with 0.1 N NaOH for 30 minutes. 0.75 ml of 0.1 N NaOH was consumed in reaction with the resulting free COOH groups. Calculated for 5 COOH groups: 0.75 ml of 0.1 N NaOH. 2 moles of base per mole of phthalylamino acid were consumed in the titration of (IV).

• No. 2 chromatograph paper from the Leningrad plant was used.

N$_6$-Phthalylvalyltriacetyladenosine (III). This compound was prepared similarly to (IV). Before analysis, the material was dried for 20 hours at 70° over P$_2$O$_5$ under vacuum.

Found %: N 12.95 C$_{29}$H$_{30}$O$_{10}$N$_6$·H$_2$O. Calculated %: N 13.1.

Tetraphthalylglycyladenosine (II). A solution of 0.27 g of anhydrous adenosine and 0.88 g of phthalyglycyl chloride in 50 ml of absolute dioxane was heated for 5 hours on a water bath. The resulting precipitate was filtered and washed with water, a 10% solution of NaHCO$_3$, and again with water. The substance was not soluble in the common organic solvents. Before analysis, the substance was dried under vacuum at 70° over P$_2$O$_5$ for 20 hours.

Found %: N 12.09. C$_{50}$H$_{33}$O$_{16}$N$_9$·H$_2$O. Calculated %: N 12.18.

Synthesis of 9-β-D-glucopyranosylguanine. 1. Acetylguanine. To a suspension of 1 g of dry, finely powdered guanine in 70 ml of freshly distilled acetic anhydride was added 2 drops of H$_3$PO$_4$. The mixture was rapidly heated to boiling on a glycerin bath. The solution became transparent after half an hour, and the heating was stopped. The acetylguanine, which precipitated when the solution was cooled, was recrystallized from dilute alcohol. M. p. 260°. The yield was 0.8 g (63.4%). Literature data for acetylguanine [10]: m. p. 260°.

2. Chloromercuri derivative of acetylguanine. To a solution of 1 g of acetylguanine in 250 ml of hot aqueous methyl alcohol was added 0.016 g of sodium hydroxide in 1 ml of water and 1.5 g of mercuric chloride dissolved in a small amount of hot methyl alcohol. The amorphous precipitate was filtered and dried in a vacuum desiccator. The yield was 1.7 g (76.7%).

3. Pentaacetylglucopyranosylguanine. The carefully ground chloromercuri derivative of acetylguanine. (1 g) was suspended in absolute xylene. Part of the xylene was distilled until the distillate became transparent. 1.5 g of acetobromoglucose [11] dissolved in xylene was added to the suspension. The solution was heated for 1 hour with vigorous stirring, and the precipitate was washed with chloroform. The chloroform and xylene solutions were combined, washed with a 30% solution of KI and then with water, dried over Na$_2$SO$_4$, and evaporated to dryness under vacuum. The remaining oil was dissolved in the minimum volume of absolute ethyl alcohol. Absolute ether was added to the solution. The precipitate was triturated 2 times with absolute ether, and was recrystallized from water. The yield was 0.5 g (42%). M. p. 295° (with decomposition). Before analysis, the material was dried under vacuum at 100° over P$_2$O$_5$ for 2 days.

Found %: C 47.04; H 5.00. C$_{21}$H$_{25}$O$_{11}$N$_5$·H$_2$O. Calculated %: C 46.60; H 5.00.

Absorption in the u. v. in phosphate buffer at a pH of 6.7: λ_{max} 261 mμ (ϵ 1140).

4. 9-β-D-glucopyranosylguanine. To a boiling solution of 0.1 g of pentaacetylglucopyranosylguanine in 1.7 ml of absolute methyl alcohol was added a hot solution of sodium alcoholate (20 mg of sodium in 1.7 ml of absolute methyl alcohol). A voluminous precipitate immediately formed. The mixture was refluxed for 1 hour, and water was then added until the precipitate completely dissolved. The solution was refluxed another 30 minutes, and allowed to stand overnight. After neutralization with 20% acetic acid, an excess of lead acetate was added. An amorphous precipitate formed when the mixture was alkalized with an aqueous solution of ammonia; the precipitate was filtered and dissolved in 7 ml of 20% acetic acid. Hydrogen sulfide was passed through the solution until precipitation of PbS was complete; the PbS was filtered and washed with water. The filtrate and wash water were evaporated to a small volume, cooled, and the resulting gelatinous precipitate was recrystallized from water. The yield was 16 mg (26.6%). M. p. 230-235° (with decomposition), R$_f$ * 0.22. U. V. absorption in phosphate buffer (pH 6.7): λ max 250, 277 mμ (ϵ 1500,11 000). According to reference [5], the m. p. is 235 (with decomposition); R$_f$ * 0.22; u. v. absorption in phosphate buffer (pH 6.7): λ_{max} 250 mμ (ϵ 13 900). 200 mg of the material was dissolved by heating in 40 ml of water, and the solution was allowed to stand overnight at room temperature; the resulting precipitate of 7-β-D-glucopyranosylguanine was filtered. The filtrate was allowed to stand for 2 days at 0°. The voluminous gelatinous precipitate of 9-β-D-glucopyranosylguanine was filtered and recrystallized 2 times from water.

U. V. absorption in phosphate buffer (pH 6.7): for 7-β-D-glucopyranosylguanine: λ_{max} 245, 280 mμ (ϵ 7900, 8900); for 9-β-D-glucopyranosylguanine: λ_{max} 250 mμ (ϵ 13 900).

Pentaphthalylglycyl-9-β-D-glucopyranosylguanine (V). A suspension of 0.1 g of 9-β-D-glucopyranosylguanine and 0.5 g of phthalylglycyl chloride in 15 ml of absolute pyridine was refluxed for 15 hours. The small

*The partition coefficient is given for the descending chromatogram in n-butanol—diethylene glycol—water (4 : 1 : 1) in an atmosphere of ammonia.

amount of precipitate was filtered. the precipitate was evaporated to dryness under vacuum, and the residue was triturated with water. The amorphous precipitate was purified by repeated precipitation from benzene with absolute ether. Before analysis, the material was dried under vacuum at 70° over P_2O_5 for 3 days.

Found %: N 11.07. $C_{61}H_{40}O_{21}N_{10} \cdot H_2O$. Calculated %: N 11.03.

Pentaphthalylphenylalanyl-9-β-D-glucopyranosylguanine (VII). This substance was prepared similarly to (V). Before analysis, the material was dried under vacuum at 70° over P_2O_5 for 3 days.

Found %: N 8.03. $C_{96}H_{70}O_{21}N_{10} \cdot H_2O$. Calculated %: N 8.15.

Pentaphthalylvalyl-9-β-D-glucopyranosylguanine (VI). The substance was prepared similarly to (V). Before analysis, the material was dried under vacuum at 65° over P_2O_5 for 13 hours.

Found %: C 60.74; H 5.13; N 9.51. $C_{76}H_{70}O_{21}N_{10} \cdot 2H_2O$. Calculated %: C 61.04; H 4.95; N 9.37.

After the material was dried under vacuum at 65° over P_2O_5 for 3 days, analysis gave the following results:

Found %: N 9.40. $C_{76}H_{70}O_{21}N_{10} \cdot H_2O$. Calculated %: N 9.49.

Hydrolysis of the acylamido derivatives of 9-β-D-glucopyranosylguanine. A solution of 30 mg of pentaphthalylglycyl-9-β-D-glucopyranosylguanine in 4.9 ml of a 0.1 N solution of sodium hydroxide was refluxed for 30 minutes. The hydrolysis product was brought to a volume of 5 ml in a volumetric flask, and 2 ml of the product was back-titrated with 0.1 N NaOH. On hydrolysis, 12 mg of the material consumed 0.96 ml of 0.1 N NaOH. The amount of 0.1 N NaOH calculated for 10 carboxyl groups is 0.97 ml. The hydrolysis product was chromatographed in n-butanol—diethylene glycol—water (4:1:1) in an atmosphere of ammonia. On development of the chromatogram under u. v., two spots were observed with R_f 0.22 and R_f 0.41. For comparison, 9-β-D-glucopyranosylguanine (R_f 0.22) and the hydrolysis product of phthalylglycine * (R_f 0.41) were placed on the chromatogram.

Similar results were obtained during the hydrolysis of pentaphthalylvalyl- and pentaphthalylphenylalanyl-9-β-D-glucopyranosylguanine.

SUMMARY

1. The syntheses of phthalylamidoacyl derivatives of adenosine and 9-β-D-glucopyranosylguanine were carried out.

2. It was established that the amine group in the purine aminonucleosides are aminoacylated under more vigorous conditions than in the cytoside nucleoside.

3. It was shown that the amide bonds in the acylamido derivatives of adenosine and 9-β-D-glucopyranosylguanine are stable toward the hydrolytic action of water, but are readily hydrolyzed by alkali (0.1 N).

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DIOXANE AND DIOXANE–BENZENE COMPLEXES OF LITHIUM-AROMATIC COMPOUNDS

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Complex compounds of aryllithium with dioxane were first prepared by us [1] by mixing a benzene solution of n-butyllithium with dioxane solutions of aryl bromides. In this preparation, the aryllithiums are formed by the exchange reaction:

$$ArBr + n\text{-}C_4H_9Li = ArLi + n\text{-}C_4H_9Br.$$

Conclusions as to the content of dioxane in the compounds obtained by this method were based on determinations of the metal in them and, in the case of derivatives of solid hydrocarbons, determinations of the hydrocarbon part. During a further investigation of the dioxane complex of 3-pyrenyllithium [2], which was prepared in a similar manner, we analyzed not only for the metal content and hydrocarbon content, but also for dioxane content. In this way, it was discovered that the complex compound of 3-pyrenyllithium contains still another substance in addition to dioxane. In connection with this observation, we carried out an additional investigation of the previously prepared complex compounds of aryllithiums to determine quantitatively the amount of dioxane in them, and it thereby became clear that in certain of these complexes the over-all amount of aryllithium and dioxane comprised 72-86% of the weight of the complex. It was natural to assume that benzene, which was used as the solvent, enters into the composition of these complex compounds [2].

TABLE 1

Dioxane Complexes of Lithium-Aromatic Compounds Prepared in a Benzene Medium

Compound	Found (in %)			Calculated (in %) for ArLi · $C_4H_8O_2$			Phthalylglycyl ArLi · $2C_4H_8O_2$		
	Li	Ar	Dioxane	Li	Ar	Dioxane	Li	Ar	Dioxane
9-Phenanthryllithium · $C_4H_8O_2$	2.35	64.03	30.48	2.55	65.09	32.36	1.93	49.18	49.89
9-Anthryllithium · $2C_4H_8O_2$	1.98	49.11	49.65	2.55	65.09	32.36	1.93	49.18	48.89

The analytical data obtained during the investigation of the complexes are presented in Tables 1 and 2; these data were not presented in our previous communication. Upon consideration of the data of Table 1, it is seen that the complex of 9-phenanthryllithium contains dioxane only in the amount of 1 molecule per molecule of aryllithium, but the complex of 9-anthryllithium includes 2 molecules of dioxane; this is in agreement with our original conclusion [1]. In Table 2 are presented data relating to analyses of complex compounds of phenyllithium, p-tolyllithium, o-tolyllithium, p-chlorophenyllithium and 3-pyrenyllithium (prepared in a benzene-dioxane medium); the analyses were carried out for lithium and dioxane content and also, in the case of the complex of 3-pyrenyllithium, for the hydrocarbon part. These data correspond to a content in the complexes of 2 molecules of dioxane and 1 molecule of benzene for 2 molecules of aryllithium compound.

TABLE 2

Dioxane—Benzene Complexes of Lithium-Aromatic Compounds Prepared in a Benzene Medium

Compound	Found (in %)		Calc. (in %) ArLi·2C$_4$H$_8$O$_2$		Calc. (in %) 2ArLi·3C$_4$H$_8$O$_2$	
	Li	Di-oxane	Li	Di-oxane	Li	Di-oxane
2C$_6$H$_5$Li·3C$_4$H$_8$O$_2$	3.40	62.01	3.21	62.04	2.66	67.71
2o-CH$_3$C$_6$H$_4$Li·3C$_4$H$_8$O$_2$	3.15	59.03	3.01	57.41	2.53	64.24
2a-C$_{10}$H$_7$Li·3C$_4$H$_8$O$_2$ *	2.86	46.95	2.61	49.63	2.24	56.77
p-CH$_3$C$_6$H$_4$Li·2C$_4$H$_8$O$_2$	2.62	64.66	3.01	57.41	2.53	64.24
p-ClC$_6$H$_4$Li·2C$_4$H$_8$O$_2$	2.57	61.17	2.77	52.62	2.36	59.81

* 1.1956 g of pyrene was obtained. Found %: C$_{16}$H$_9$ 59.39. 2C$_{16}$H$_9$Li·2C$_4$H$_8$O$_2$·C$_6$H$_6$. Calculated %: C$_{16}$H$_9$ 60.01

For proof of the presence of benzene in the above-indicated complex compounds, one of them — the complex of p-chlorophenyllithium — was prepared in considerable quantity (starting with 0.1 mole of p-chloro-bromobenzene), and was subjected to complete analysis. The complex of p-chlorophenyllithium, which was prepared in a benzene medium in the presence of dioxane, was carefully washed with isopentane, freed from traces of the latter under vacuum (3 mm) at room temperature, and decomposed. From the hydrolysis products was separated 2.2 g of benzene, which corresponds to 67.6% of the theoretical benzene content considering the complex to have the composition 2 ClC$_6$H$_4$Li·2C$_4$H$_8$O$_2$·C$_6$H$_6$. Hence, it can be concluded that the complex compounds of phenyllithium, p-tolyllithium, o-tolyllithium, and 3-pyrenyllithium when prepared in benzene medium in the presence of dioxane, which, according to the analytical data, have the composition 2ArLi·2C$_4$H$_8$O$_2$·C$_6$H$_6$. are dioxane—benzene complexes. The structure of these compounds can be represented by the following structural formula (I), which reflects the π-complex nature of the bonds of the benzene molecule with the lithium atoms.
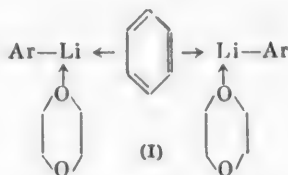

It should be pointed out that the ability of aromatic hydrocarbons to add to organic and heteroorganic compounds has been noted in a number of cases. Thus, benzene forms complex compounds with triphenylmethyl [3], trinaphthylboron [4], and nickel cyanide [5].

In order to clarify the effect of the medium on the complex-forming ability of lithium-aromatic compounds with respect to dioxane, we studied complexes of aryllithiums prepared in n-hexane solution in the presence of dioxane. An amount of an n-hexane solution of n-butyllithium corresponding to 1 equivalent of n-butyllithium was added to a solution of the aryl bromide in a mixture of n-hexane and dioxane, the latter being present in an amount of 4 equivalents. The complex, which precipitated from the solution, was filtered, washed with n-hexane, freed from solvent under vacuum, and analyzed for lithium and dioxane content. The data obtained are presented in Table 3.

As seen from the analytical data, phenyllithium, o-tolyllithium, and α-naphthyllithium form, in n-hexane medium, complexes with dioxane having the composition 2 ArLi·3C$_4$H$_8$O$_2$, which are analogous in composition to the dioxane complex of 3-pyrenyllithium prepared in ether medium [2].

The structure of these complex compounds can be represented by structural formula (II).

In a hexane medium, p-tolyllithium and p-chlorophenyllithium form bis(dioxane) complexes (III), ArLi· ·$2C_4H_8O_2$, which are analogous to the complex of 2-anthryllithium prepared in benzene medium.
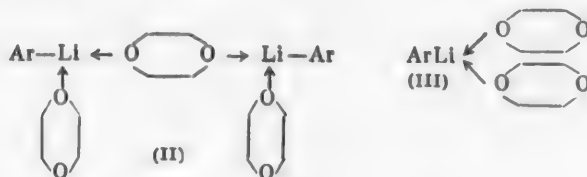
Thus, in the above-enumerated complex compounds, lithium has the coordination number 3.

TABLE 3

Dioxane Complexes of Lithium-Aromatic Compounds Prepared in an n-Hexane Medium

Compound	Found (in %)			Calculated (in %) for $2ArLi \cdot 2C_4H_8O_2 \cdot C_6H_6$		
	Dioxane	Di-oxane	Ben-zene (by diff.)	Dioxane	Ben-zene (by diff.)	Ben-zene (by diff.)
$2C_6H_5Li \cdot 2C_4H_8O_2 \cdot C_6H_6$	3.20	43.22	18.02	3.28	41.72	18.49
$2p\text{-}CH_3C_6H_4Li \cdot 2C_4H_8O_2 \cdot C_6H_6$	3.23	38.82	15.59	3.07	39.10	17.37
$2o\text{-}CH_3C_6H_4Li \cdot 2C_4H_8O_2 \cdot C_6H_6$	3.23	40.90	13.51	3.07	39.10	17.37
$2p\text{-}ClC_6H_4Li \cdot 2C_4H_8O_2 \cdot C_6H_6$	2.74	36.32	15.96	2.82	35.88	15.89
$2(3\text{-pyrenyllithium}) \cdot 2C_4H_8O_2 \cdot C_6H_6$ *	1.90	26.00	9.26	2.07	26.55	11.64

* 0.9533 g of naphthalene was obtained. Found %: $C_{10}H_7$ 45.56. $2C_{10}H_7Li \cdot 3C_4H_8O_2$.
Calculated %: $C_{10}H_7$ 47.74

As the experimental data show, the nature of the solvent has an effect on the complex-forming ability of lithium-aromatic compounds with respect to dioxane. Phenyllithium adds 1 molecule of dioxane in ether medium [2], while it has now been found that in hexane medium 2 molecules of phenyllithium are combined with 3 molecules of dioxane (Table 3).

p-Tolyllithium also adds less dioxane in ether solution than in hexane. When 4 equivalents of dioxane are added to an ether solution of p-tolyllithium a complex separates which contains 3 molecules of dioxane per 2 molecules of aryllithium (see Experimental), while in a hexane medium, p-tolyllithium forms the bis(dioxane) complex (Table 3); in an ether medium, α-naphthyllithium forms the monodioxane complex [2], but when n-hexane is used as the solvent, the dioxane complex has the composition $2\alpha\text{-}C_{10}H_7Li \cdot 3C_4H_8O_2$ (Table 3).

It should be pointed out that, owing to its simplicity, the method described by us for the preparation of dioxane and dioxane—benzene complexes is of value in planning syntheses, especially for compounds of the benzene series. In the form of ether solutions, the complexes can be used for various synthesis operations in which it is not desirable to use aryllithiums in a mixture with an equimolar amount of the lithium halide (during the preparation of the aryllithiums from lithium and aryl halides).

T. V. Talalaeva, M. M. Nad' and K. A. Kocheshkov [6] reported that when repeating our experiment on the synthesis of complex compounds by the action of n-butyllithium on aryl bromides in benzene—dioxane solution, they obtained precipitates with high contents of lithium bromide (28-42%). The authors obtained these results, because they took no precautions against the heat evolved from the reaction mixture; this heat favors the formation of lithium bromide by a secondary reaction between the aryllithium and butyl bromide. When the same reaction is carried out under mild conditions, namely, cooling with ice water and slow stirring of the reagents, the complex compounds which separate from the solution contain only traces of lithium bromide. In

the article cited [1], we did not give the experimental details, but we did point out in other communications [2, 7] the necessity for cooling during the preparation of complex compounds of aryllithiums by an exchange reaction between aryl bromides and butyllithium.

In this same article, Talalaeva, Nad' and Kocheshkov wrote that it was not clear to them why Mikhailov and Aranovich [8], in describing the preparation of phenyllithium from triphenylantimony and n-butyllithium, found it more convenient to refer to the article of Woods and Gilman [9] and not to their work [10]. The authors are clearly in error here. In actuality, Mikhailov and Aranovich made reference both to the work of Woods and Gilman, in which the reaction between triarylantimony and n-butyl lithium was described, and the article of Talalaeva and Kocheshkov, which was devoted to the development of a method of preparation of individual lith-ium-aromatic compounds from triarylantimony and ethyllithium on the basis of the Woods and Gilman reaction mentioned above. Moreover, it was pointed out that Talalaeva and Kocheshkov, while using in their work the reaction of Woods and Gilman did not so refer to it. Talalaeva and Kocheshkov have also described as original with them a method for the preparation of triarylantimony compounds from antimony trichloride and aryllithiums [11], while in actuality their work was a development of an idea by Woods, a student of Gilman's, who first pro-posed to prepare triarylantimony compounds by such a method [12].

EXPERIMENTAL

Analysis of the complex compounds. Analysis of the complex compounds was carried out by the previously described method [2]. In the determination of dioxane, a correction was introduced for the solubility of the diox-ane—mercuric chloride complex in water saturated with ether at room temperature, which is equal to 1.03 g in 100 ml of solution at 0°.

Preparation of n-butyllithium. To a two-armed ampoule filled with nitrogen were charged 2.3 g of finely shaved lithium, 16 ml of n-butyl chloride, 80 ml of benzene, and glass beads; the ampoule was sealed and was shaken on a rocker for 15-20 hours. The solution was filtered into a cylindrical vessel, which was connected by means of a ground-glass joint to a 15-ml buret. The solution contained 1.3-1.4 moles of n-butyllithium per li-ter. The n-hexane solution of n-butyllithium was prepared similarly.

Preparation of dioxane and dioxane—benzene complexes of lithium-aromatic compounds in a benzene medium. All operations with lithium-aromatic compounds were carried out in an atmosphere of nitrogen. The following were used in the experiments: 1) 16 mmole of bromobenzene and 64 mmole of dioxane, 2) 10 mmole. of p-bromochlorotoluene and 40 mmole of dioxane 3)10 mmole of o-bromotoluene, 3.5 mmole of dioxane, and 5 ml of benzene, 4) 10 mmole of 3-bromopyrene, 70 mmole of dioxane, and 6 ml of benzene, 5) 7 mmole of 9-bromophenanthrene and 28 mmole of dioxane, 6) 8 mmoles of 9-bromoanthracene and 93 mmole of dioxane. The majority of the complexes were prepared by adding a dioxane or benzene—dioxane solution of the aryl bromide to a benzene solution of n-butyllithium. The preparations were carried out in a single-necked vessel having a volume of 75 ml and fitted with a side arm with a glass stopcock through which nitrogen was introduced. The neck of the vessel was connected through a ground-glass joint to a glass stopcock; the vessel was filled with ni-trogen, the stopcock was removed, and the end of a buret was inserted into the flask through a stopper. A ben-zene solution of n-butyllithium was introduced into the vessel from the buret, the solution was cooled with ice water, and a solution of an equimolar amount of aryl bromide was slowly added dropwise and with stirring. The complexes of o-tolyllithium and 9-phenanthryllithium were prepared by the addition of a benzene solution of an equimolar amount of n-butyllithium to a solution of aryl bromide while cooling the reaction mixture with ice water.

At the conclusion of the mixing of the reagents, the vessel was closed, allowed to stand for 10 minutes in ice water, and the precipitated complex was filtered in a special filtering funnel [7]. For the filtration, the cyl-indrical head was inserted by means of a ground-glass joint into the neck of the reaction vessel, and was connect-ed through rubber tubing to the head of the filtering funnel. The filtered complex was twice washed with ben-zene, and was freed from solvent under vacuum (3 mm) at room temperature to constant loss in weight. For this purpose, the dioxane—benzene complexes of lithium-aromatic compounds of the benzene series had to be main-tained under vacuum for a period of 2-3 hours, and the constant loss in weight of these compounds was 7-8 mg in 10 minutes (in our first work [1], these complexes were maintained under vacuum for about 1 hour). The com-plex of 3-pyrenyllithium was maintained under vacuum for 1 hour, after which the loss in weight comprised 1-2 mg in 10 minutes. The dioxane complexes of 9-phenanthryllithium and 9-anthryllithium were more stable, and

they attained almost constant weight over a period of 30-60 minutes. The dioxane —benzene complex of o-tolyllithium was washed with pentane; in this case, a constant loss in weight of 3-4 mg in 5 minutes was attained over a period of 30 minutes.

The complex compounds prepared by this method contained 0.2-0.5% lithium bromide as an impurity.

In the majority of cases, the yields of complexes comprised 75-82% of theoretical; the yields of complexes of o-tolyllithium and 3-pyrenyllithium were 51.6 and 56.7%, respectively.

Preparation of the dioxane —benzene complex of p-chlorophenyllithium for the purpose of identifying benzene in it. The reaction vessel was a three-necked flask into which were inserted, through rubber stoppers, a buret containing a benzene solution of n-butyllithium and a thermometer extending to the bottom of the flask; the third neck was connected to a length of rubber tubing. To the flask, which was filled with nitrogen, was charged a solution of 23 g (0.12 mole) of p-bromochlorobenzene in a mixture of 17.6 ml (0.2 mole) of dioxane and 70 ml of benzene; the solution was cooled to + 3° with ice water, and 68 ml of a benzene solution of n-butyllithium (0.1 mole) was added dropwise over a period of 40 minutes. The temperature in the reaction mixture was maintained within the limits 3-7°. At the conclusion of the addition of the n-butyllithium, the center neck of the flask was closed with a stopper; the second neck served for the introduction of nitrogen, and a cylindrical head, which was connected by means of rubber tubing to the head of the special filtering funnel [7] (150 ml volume), was inserted through a ground-glass joint into the third neck. The precipitate was filtered, washed 3 times with isopentane (150 ml), and then was subjected to a vacuum (3 mm) for 2.5 hours to free it from solvent (the weight loss was 9 mg in 10 minutes). 20.3774 g of the complex was obtained (yield 85%).

70 ml of ether was added to the funnel; the funnel was then submerged in ice water, and the complex was decomposed with methanol, which was introduced through the periodically opened upper stopcock of the funnel. At the conclusion of the alcoholysis, water was added, and the mixture was shaken and transferred to a separatory funnel; the filtering funnel was washed with water. The ether solution was extracted 3 times with water. The total volume of the aqueous solution was 250 ml. The ether solution was then agitated with an aqueous solution (20 ml) of 1 g of mercuric chloride, and the aqueous layer was separated and cooled with ice. The resulting dioxane —mercuric chloride complex was included in the over-all dioxane balance.

The lithium and dioxane contents of the main aqueous solution were determined in an aliquot of the solution.

Found %: Li 2.61; dioxane 32.61. $2ClC_6H_4Li \cdot 2C_4H_8O_2 \cdot C_6H_6$. Calculated %: Li 2.74; dioxane 35.88.

The ether solution was fractionally distilled in a column. 2.2 g of benzene, b. p. 80°, n_D^{20} 1.501, was obtained, which corresponded to 67.6% of the theoretical benzene content of the complex. Nitration of 1.6 g of the fraction boiling at 80° gave 2.1 g of m-dinitrobenzene with an m. p. of 88-89°.

Preparation of dioxane complexes of lithium —aromatic compounds in n-hexane medium. In the experiments on the preparation of complexes of phenyllithium, o-tolyllithium and α-naphthyllithium, 10 mmole of the corresponding bromides was used per 40 mmole of dioxane; in the preparation of complexes of p-tolyllithium and p-chlorophenyllithium, 7 mmole of the aryl bromide was used per 28 mmole of dioxane. The aryl bromide was dissolved in a mixture of dioxane and 10 ml of n-hexane, the solution was cooled with ice water, and an n-hexane solution of an equimolar amount of n-butyllithium was added dropwise and with stirring. The precipitated complex was filtered, washed with hexane, freed from solvent by subjecting to a vacuum for 30 minutes (the weight loss was 1-2 mg in 5 minutes), and analyzed (see Table 3). The complex compounds contained traces of lithium bromide.

The yields of complex compounds were (in % of theoretical): phenyllithium, 62.8; o-tolyllithium, 41.7; α-naphthyllithium, 77.8; p-tolyllithium, 48.3; p-chlorophenyllithium, 61.

When the dioxane and dioxane —benzene complexes are to be prepared in quantity, 2 equivalents of dioxane can be used; it is expedient to carry out the washing of the complexes with isopentane.

Preparation of p-tolyllithium —dioxane complex in ether medium. $2CH_3C_6H_4Li \cdot 3C_4H_8O_2$. The p-tolyllithium was prepared by the Gilman and Woods reaction from tri-p-tolylantimony and n-butyllithium [10]. The use of ethyllithium for this purpose, as proposed by Talalaeva and Kocheshkov [11], is less satisfactory owing to the laborious method required for its preparation [13]. 24 ml of a benzene solution of n-butyllithium (30 mmole)

was added to 4 g (10 mmole) of tri-p-tolylantimony dissolved in 15 ml of benzene. The solution was heated on a water bath at 40-45° for 40 hours. The resulting crystalline precipitate was filtered in the special filtering funnel, washed with pentane, and freed from solvent under vacuum. 2.13 g (72.4%) of p-tolyllithium was obtained. The p-tolyllithium was dissolved in 15 ml of ether, the solution was filtered from the slight suspension, and 3.7 ml (43 mmole of dioxane was added to it; the solution was cooled with ice during the addition. The precipitated complex was filtered, washed 3 times with pentane, and held under vacuum (3 mm) for 40 minutes to a constant loss in weight of 3-4 mg in 5 minutes. 4.2257 g (84.7%) of the complex was obtained.

2.1730 g substance: 0.0926 g Li; 1.2400 g dioxane. Found %: Li 3.00, dioxane 57.06. $2C_7H_7Li \cdot 3C_4H_8O_2$. Calculated %: Li 3.01; dioxane 57.41.

SUMMARY

1. Dioxane—benzene complexes of lithium-aromatic compounds, with the composition $2ArLi \cdot 2C_4H_8O_2 \cdot C_6H_6$, are formed by the action of a benzene solution of n-butyllithium on aryl bromides in the presence of dioxane. Phenyllithium, p-tolyllithium, o-tolyllithium, p-chlorophenyllithium, and 3-pyrenyllithium form complexes of this composition.

2. Under the conditions indicated above, 9-phenanthryllithium and 9-anthryllithium form dioxane complexes of the composition $ArLi \cdot C_4H_8O_2$ and $ArLi \cdot 2C_4H_8O_2$, respectively.

3. Dioxane complexes of the composition $2ArLi \cdot 3C_4H_8O_2$ or $ArLi \cdot 2C_4H_8O_2$ are formed by the action of an n-hexane solution of n-butyllithium on aryl bromides in the presence of dioxane.

4. The nature of the solvent has an effect on the composition of dioxane complexes of lithium-aromatic compounds. Aryllithiums form complexes with a lower dioxane content in an ether medium than in a hexane medium.

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QUATERNARY SALTS OF N-MONOXIDES OF PHENAZINE AND QUINOXALINE DERIVATIVES

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Like tertiary amines, quinoline pyridine, phenazine, quinoxaline, and their derivatives react with per acids to form the corresponding N-monoxides and N,N-dioxides. In reactions with alkyl halides or dialkyl sulfates, they form quaternary salts. The quaternary salts of derivatives of pyrazine have as yet been neither investigated nor prepared. The present article describes reactions by which quaternary salts of N-oxides of phenazine, quinoxaline, and some of their derivatives are formed, and the properties of these new compounds.

On heating the N-oxides of phenazine or its α- or β-derivatives in solution in dry nitrobenzene with a small excess of neutral dimethyl sulfate, good yields of the corresponding quaternary salts are obtained

or $R = Cl, CH_3, OCH_3$.
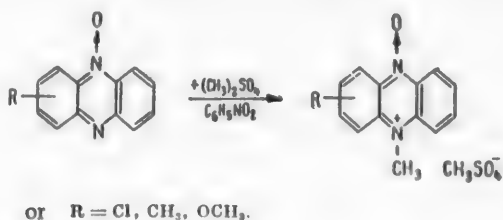
Quinoxaline derivatives react in a similar manner. The reaction by which the quaternary salts of the N-oxides are formed proceeds smoothly at 115-130°, and is, for the most part, complete within 8-10 minutes. The end of the reaction is established from the solubility of the reaction product in cold water and from the changed form and color of the resulting crystals: phenazine N-oxide and its derivatives are yellow needles which are insoluble in water; crystals of the quaternary salts of these same N-oxides are red or bright orange prisms or plates which are readily soluble in water. When the reaction mixture is cooled, the major part of it immediately precipitates in the form of crystals; the precipitate is washed on the filter with benzene and absolute ether, and is then purified by crystallization from alcohol or water. The quaternary salts (methyl sulfates) of the N-oxides of phenazine and quinoxaline are readily soluble in water, difficultly soluble in alcohol, nitrobenzene, and pyridine, and sparingly soluble in chloroform; they are insoluble in benzene, ether, and ligroin. They are characterized by stable melting points and decomposition temperatures. Crystals of the quaternary salts of the N-oxides, like phenazine N, N-dioxides, are bright orange or red, possibly owing to a certain similarity in the structures of their molecules.
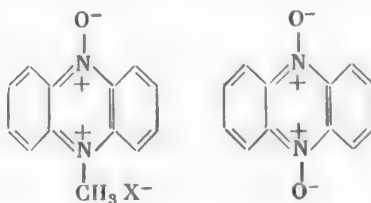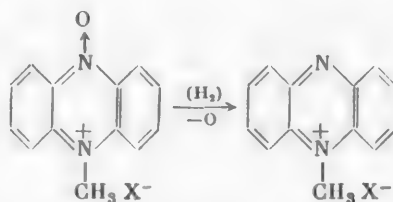
The quaternary salts of phenazine N-oxides are readily oxidized by potassium ferricyanide in alkaline solution, thereby forming phenazinones, which have a red or violet color and are readily soluble in chloroform, alcohol, and dichloroethane. The simplest of them can be represented by the following structure.
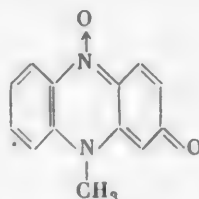
In acids, the phenazinone N-oxides form the corresponding hydroxyphenazinium quaternary salts, the spectra of which lie much further in the short-wave region than do the spectra of the corresponding phenazinones; for example, an alcohol solution of the phenazinone obtained by oxidation of the 10-oxide of 2-chloro-9-methylphenazinium methyl sulfate has an absorption maximum at 518 mμ, while in acidified alcohol, the maximum occurs at 432 mμ.

The absorption spectrum of quaternary salts of phenazine N-oxide is characterized by three absorption bands with maxima at 259, 310, and 385 mμ. The band at 310 mμ is not present in the spectrum of phenazine quaternary salts. Oxidation of the quaternary salt of phenazine with 20% hydrogen peroxide in glacial acetic acid gives a product, the spectrum of which conforms to the spectrum of the quaternary salt of phenazine N-oxide; the oxidation results in the appearance in the spectrum of a band at 310 mμ.

The possibility of forming N-methoxyphenazinium methyl sulfate during the action of dimethyl sulfate on phenazine oxide in nitrobenzene could not be ignored, but the compound was not detected in the separated reaction products, though the formation of such products were observed by Henze during the action of methyl iodide on quinoline oxide [1] and by Katritzky during the methylation of pyridine N-oxide [2]. Apparently, in nitrobenzene, the N-monoxides of the dinitrogen heterocyclic compounds of the pyrazine series add the alkyl group to the free nitrogen atom, rather than to the oxygen. Proof of this is the reaction by which quaternary salts of N-oxides of phenazine and its derivatives are converted by reduction by zinc dust in cold water to the ordinary phenazinium quaternary salts.

The following phenazine and quinoxaline N-oxides were converted to quaternary salts (methyl sulfate and perchlorate) by the method described above: the 9-oxides of phenazine and 2-methyl-, 2-methoxy, and 2-chlorophenazines; the 10-oxides of 1-methyl-, 2-methoxy-, 2-chloro-, and 2-chloro-6-methoxyphenazine; the 1-oxide of 2,3-diphenylquinoxaline; the 1-(or 4-)oxide of 2,3-diphenyl-7-methylquinoxaline; the 1-oxide of 2,3-acenaphthylenoquinoxaline; and the 1-(or 4-)oxide of 2,3-acenaphthyleno-7-methylquinoxaline. Data on these quaternary salts of phenazine and quinoxaline N-oxides are presented in Tables 1 and 2.
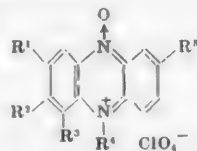
EXPERIMENTAL

10-Oxide of 9-methylphenazinium perchlorate (I). 1 g of the N-oxide of phenazine in 2.5 ml of dry nitrobenzene was heated at 120-125° until completely dissolved, 1.5 ml of neutral dimethyl sulfate was added, and heating was continued for 10 minutes at 125-128°; the solution was then cooled, the precipitate filtered and washed with benzene and ether, dissolved in 10 ml of water, and heated with activated carbon; the filtrate was treated with sodium perchlorate to precipitate the product. The yield was 1.3 g of orange prisms. Part of the product, after isolation, was oxidized to phenazinone with potassium ferricyanide in alkaline solution.

according to the method of McIlwain [3], and the product was extracted with chloroform. The phenazinone was red, and had an absorption maximum at 522 mμ.

The 10-Oxide of 1,9-dimethylphenazinium perchlorate (II) was prepared similarly to the preceding compound, but the heating was at 105-110° for 5 minutes. The product was in the form of light-orange crystals. The phenazinone had an absorption maximum at 520 mμ.

TABLE 1

Quaternary Salts of Phenazine N-Monoxides

Expt. No.	R¹	R²	R³	R⁴	R⁵	Melting point (decomp.)	Yield (%)	Empirical formula	Found %		Calculated %	
									N	Cl	N	Cl
I	H	H	H	CH_3	H	214	81	$C_{13}H_{11}N_2O_5Cl$	8.96, 8.97	11.72, 11.76	9.01	11.43
II	H	H	CH_3	CH_3	H	200	53	$C_{14}H_{13}N_2O_5Cl$	—	10.71, 10.64	—	10.94
III	CH_3	H	H	CH_3	H	196	41	$C_{14}H_{13}N_2O_5Cl$	8.59, 8.49	10.77, 10.89	8.63	10.94
IV	CH_3O	H	H	CH_3	H	204	41	$C_{14}H_{13}N_2O_6Cl$	8.55, 8.60	10.28, 10.65	8.22	10.42
V	H	CH_3O	H	CH_3	H	198	40	$C_{14}H_{13}N_2O_6Cl$	8.13, 7.89	10.39, 10.60	8.22	10.42
VI	Cl	H	H	CH_3	H	220	60	$C_{13}H_{10}N_2O_5Cl_2$	8.01, 7.88	20.80, 20.73	8.11	20.58
VII	H	Cl	H	CH_3	H	223	70	$C_{13}H_{10}N_2O_5Cl_2$	8.14, 7.83	20.52, 20.73	8.11	20.58
VIII	H	Cl	H	CH_3	CH_3O	213	76	$C_{14}H_{12}N_2O_6Cl_2$	7.54, 7.50	18.88	7.47	18.93

9-Oxide of 2,10-dimethylphenazinium perchlorate (III). 1 g of 2-methylphenazine 9-oxide in 2 ml of nitrobenzene was heated to 90° on a water bath, and 1.2 ml of dimethyl sulfate was then added. The temperature rose to 118° owing to exothermic heat of reaction. The reaction mixture was held at this temperature for 3 minutes. The product was crystallized from water.

9-Oxide of 2-methoxy-10-methylphenazinium perchlorate (IV). 2 g of 2-methoxyphenazine 9-oxide in 2 ml of nitrobenzene was mixed at 110° with 1.5 ml of dimethyl sulfate, and heating was continued for 10 minutes at 115°. The reaction mixture was washed with toluene and ether, dissolved in 5 ml of water, treated with activated carbon, and filtered; the product was precipitated with sodium perchlorate. The quaternary salt was crystallized from water as orange needles. It was quite readily oxidized to the phenazinone, which had an absorption maximum at 520 mμ.

The 10-oxide of 2-methoxy-9-methylphenazinium perchlorate (V) was prepared in a manner similar to the preceding from 2-methoxyphenazine 10-oxide and dimethyl sulfate; the reaction mixture was heated at 110-113° for 5 minutes. The product was in the form of red needles (from water).

The 9-oxide of 2-chloro-10-methylphenazinium perchlorate (VI) was prepared in a manner similar to the above from 2-chlorophenazine 9-oxide. The product was in the form of orange plates. The phenazinone was violet.

The 10-oxide of 2-chloro-9-methylphenazinium perchlorate (VII) was prepared in a manner similar to the above from 2-chlorophenazine 10-oxide. The resulting plates were orange colored. The phenazinone was red with an absorption maximum at 518 mμ.

10-Oxide of 2-chloro-6-methoxy-9-methylphenazinium perchlorate (VIII). 2 g of 2-chloro-6-methoxy-phenazine 10-oxide in 8 ml of nitrobenzene was heated for 2 minutes at 125°, 4 ml of dimethyl sulfate was added, and heating was continued for 15 minutes at 125-130°. Further treatment was as usual. Orange, almost red hexagonal plates (from water) resulted. The phenazinone was red.

1-Oxide of 2,3-diphenyl-4-methylquinoxalinium perchlorate (IX). 3 ml of dimethyl sufate was added to 2.9 g of 2,3-diphenylquinoxaline 1-oxide in 4 ml of nitrobenzene at 125-130°, and this temperature was maintained for 15 minutes. The quaternary salt was washed with benzene and ether, dissolved in 10 ml of water, and treated with sodium perchlorate to precipitate the product. Light-orange needles resulted (from alcohol).

TABLE 2

Quaternary Salts of Quinoxaline N-Monoxides
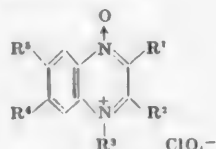
Expt. No.	R^1	R^2	R^3	R^4	R^5	Melting point (decomp.)	Yield (in %)	Empirical formula	Found (%)		Calculated (%)	
									N	Cl	N	Cl
IX	C_6H_5	C_6H_5	CH_3	H	H	177	96	$C_{21}H_{17}N_2O_5Cl$	6.55, 6.45	8.37, 8.57	6.78	8.60
X	C_6H_5	C_6H_5	CH_3	H	CH_3	220	80	$C_{22}H_{19}N_2O_5Cl$	6.59, 6.43	—	6.56	—
XI			CH_3	H	H	246	71	$C_{20}H_{16}N_2O_5S$ *	7.12, 6.98	—	7.07	—
								$C_{19}H_{13}N_2O_5Cl$	—	9.30, 9.40	—	9.23
XII			CH_3	H	CH_3	232	43	$C_{20}H_{15}N_2O_5Cl$	6.93, 7.02	—	7.03	—

*Methyl sulfate.

The 1-oxide of 2,3-diphenyl-4,7-(or 4,6-)-dimethylquinoxalinium perchlorate (X) was prepared from 1 g of 2,3-diphenyl-7-methylquinoxaline 1-(or 4-)-oxide in a manner similar to that described above. It was in the form of orange, almost yellow, prisms.

1-Oxide of 2,3-acenaphthyleno-4-methylquinoxalinium perchlorate (XI). 1.35 g of 2,3-acenaphthyleno-quinoxaline 1-oxide was heated in 5 ml of nitrobenzene for 15 minutes at 125°; 2 ml of dimethyl sulfate was then added, and heating was continued for 5 minutes at 125-130°. The reaction mass completely crystallized at 120°, and it was washed with benzene and ether. The product was recrystallized from alcohol in the form of yellow needles.

The 1-oxide of 2,3-acenaphthyleno-4,7-(or 4,6-)-dimethylquinoxalinium perchlorate (XII) was prepared in a manner similar to that described above from 0.5 g of the 1-(or 4-)-oxide of 2,3-acenaphthyleno-7-methyl-quinoxaline. Formation of the salt proceeded easily and rapidly. Treatment of the product was as usual. The product was in the form of yellow needles. When heated, the salt decomposed explosively.

Phenazine and Quinoxaline Monoxides

Phenazine 9-oxide. 40 ml of 20% hydrogen peroxide was added dropwise, with stirring and over a period of 4 hours, to 18 g of phenazine in 200 ml of glacial acetic acid at 60-75°. The cooled solution was diluted with 1 liter of water. The resulting light-orange precipitate was filtered, washed with water, and dried. The

yield was 17.5 g. It was chromatographed in chloroform solution on aluminum oxide; the column was eluted with benzene. From the lower, yellow zone was obtained 5 g (25%) of phenazine 9-oxide with an m. p. of 219-220° (224-225° [4]). From the upper, orange zone was obtained 12 g (29%) of phenazine 9,10-dioxide with an m. p. of 189-191° [4]. •

1-Methylphenazine 10-oxide was prepared by the Wohl method from o-toluidine and nitrobenzene [5]. The product was in the form of yellow needles with an m. p. of 195°. It was purified by chromatographing on aluminum oxide from benzene solution.

2-Methylphenazine 9-oxide. 20 ml of 20% hydrogen peroxide was added dropwise, over a period of 4 hours, to 7.8 g of 2-methylphenazine in 100 ml of glacial acetic acid at 50-60°. Further treatment of the product was as indicated above for phenazine 9-oxide. 2 g (23%) of unoxidized 2-methylphenazine was obtained from the lower zone of the chromatogram. From the central zone was obtained 2.02 g (24%) of 2-methylphenazine 9-oxide with an m. p. of 138°. This monoxide was identified by comparison with 2-methylphenazine 9-oxide prepared by the Wohl method [5] —alkaline condensation of p-toluidine and nitrobenzene in benzene. 0.5 g (5.5%) of 2-methylphenazine 9,10-dioxide with an m. p. of 170° was obtained from the upper layer of the chromatogram.

2-Methoxyphenazine 9-oxide was prepared, in 12% yield, by alkaline condensation of p-anisidine and nitrobenzene in benzene solution. The m. p. was 179°. The product was purified by chromatographing in benzene solution on aluminum oxide and recrystallization from benzene (m. p. 179° [6]).

2-Methoxyphenazine 10-oxide. This preparation was presented to us by S. B. Serebryanyi. The m. p. was 175° (from benzene).

2-Chlorophenazine 10-oxide was prepared by alkaline condensation of p-chloronitrobenzene and aniline in benzene solution; the yield was 12%. The compound was purified by chromatographing a benzene solution on aluminum oxide. The m. p. was 176-178° (from benzene).

2-Chlorophenazine 9-oxide was prepared in a manner similar to that described above from p-chloroaniline and nitrobenzene; the yield was 16.4%. The product was purified by chromatographing on aluminum oxide. The m. p. was 178-179°. The product was in the form of yellow needles.

2,3-Diphenylquinoxaline 1-oxide. 40 ml of 20% hydrogen peroxide was added dropwise, over a period of 4 hours with stirring, to 14 g of 2,3-diphenylquinoxaline in 200 ml of glacial acetic acid at 60-80°. The colorless solution became yellow. The reaction mixture was poured into 1 liter of water. This caused separation of a viscous yellow material, which solidified on standing. It was ground in a mortar with cold water until it was completely pulverized; it was then filtered, washed on the filter with water, and dried. The yield was quantitative. The compound was purified by chromatographing a chloroform solution on aluminum oxide and eluting the column with benzene. The yield of purified product was 12 g (80%). The m. p. was 207° (from alcohol).

Found %: N 9.28, 8.90. $C_{20}H_{14}ON_2$. Calculated %: N 9.39.

2,3-Diphenyl-7-methylquinoxaline 1-(or 4)-oxide. This compound was prepared in a manner similar to that described above from 6 g of 2,3-diphenyl-7-methylquinoxaline; the oxidation was carried out at 60-70° with 20 ml of hydrogen peroxide. The yield was 5.6 g (89%). Chromatographing on aluminum oxide gave pale-yellow needles with an m. p. of 178-180° (from alcohol).

Found %: N 8.78, 8.93. $C_{21}H_{16}ON_2$. Calculated %: N 9.00.

2,3-Acenaphthylenoquinoxaline 1-oxide was prepared in a manner similar to that described above from 2.54 g of 2,3-acenaphthylenoquinoxaline; the oxidation was carried out with hydrogen peroxide (20 ml) at 50-75°. The suspended material went into solution when the hydrogen peroxide was added. Heating was continued for 3.5 hours. Toward the end of the reaction, an abundant, bright-yellow precipitate of the N-oxide began to form. The yield was 2.7 g (100%). The product was very pure, and did not require further purification. The long, bright-yellow needles melted at 224°. The compound crystallized from 50% acetic acid as small yellow needles with water of crystallization, which was lost on drying (100-130°); this resulted in a change in the color of the preparation from yellow to orange. Recrystallization from glacial acetic acid gave orange crystals.

Found %: N 10.30, 10.11. $C_{18}H_{10}ON_2$. Calculated %: N 10.37.

•The m.p. from [4] has apparently been omitted — Publisher's note.

2,3-Acenaphthylenoquinoxaline 1-(or 4)-oxide was prepared in a manner similar to that described above from 2,3-acenaphthylenoquinoxaline; the yield was 100%. Purification on aluminum oxide (chromatographically) gave samll, yellow needles with an m. p. of 262°.

Found %: N 9.62, 9.82. $C_{19}H_{12}ON_2$. Calculated %: N 9.85.

Reduction of the quaternary salt of phenazine N-oxide. 1.6 g of the N-oxide of phenazinium methyl sulfate was dissolved in 10 ml of water, and the solution was filtered; 1 g of zinc dust was added, and the mixture was stirred in a test tube with a thermometer. The temperature increased to 50° over a period of 3-5 minutes. The orange solution gradually became yellow. When the orange color had disappeared, the solution was filtered from the zinc dust, and the product was precipitated with sodium perchlorate. The yield of phenazine quaternary salt was 0.8 g (57%). The m. p. was 200-201°. A mixture of this material with a known sample melted at 200°.

Found %: N 9.50, 9.52. $C_{13}H_{11}N_2ClO_4$. Calculated %: N 9.51.

Reduction of the quaternary salt of 2-chloro-6-methoxyphenazine 10-oxide. 0.65 g of the 10-oxide of 2-chloro-6-methoxy-9-methylphenazinium methyl sulfate in 12 ml of water was reduced, in a manner similar to that described above, with 1 g of zinc dust at 25-31° for 7 minutes. The yield was 0.32 g (51%). The resulting brown needles melted at 198°.

Found %: N 7.81, 7.96; Cl 19.65, 19.82. $C_{14}H_{12}O_5N_2Cl_2$. Calculated %: N 7.79; Cl 19.54.

Reduction of the quaternary salt of 2-chloro-9-methylphenazine 10-oxide. 1.15 g of 2-chlorophenazine 10-oxide was converted to 2-chloro-9-methylphenazinium methyl sulfate by the method described above; yield was quantitative (1.7 g). The salt was dissolved in 15 ml of water, treated with activated carbon, filtered, and mixed with 1.6 g of zinc dust. The yield of 2-chloro-9-methylphenazinium perchlorate was 31%. The m. p. was 188° (decomp.).

Found %: N 8.63, 8.64; Cl 21.55. $C_{13}H_{10}O_4N_2Cl_2$. Calculated %: N 8.51; Cl 21.58.

9-Methylphenazinium perchlorate. 2 g of phenazine in 6 ml of nitrobenzene was heated at 120-125° for 5 minutes; 2 ml of dimethyl sulfate was then added, and heating was continued for another 5 minutes at 125-130°. The reaction mixture was cooled, filtered, and washed with benzene and ether. The yield was 2.1 g (61%). The compound was converted to the perchlorate, which was purified by 3-fold crystallization from alcohol. The olive-yellow plates melted at 202° (decomp.).

Found %: N 9.50, 9.52. $C_{13}H_{11}O_4N_2$ Cl. Calculated %: N 9.50.

The spectral measurements were carried out with SF-4 and SF2M instruments. The melting points reported for the compounds are uncorrected.

SUMMARY

It was shown that it is possible to convert phenazine and quinoxaline N-oxides to the corresponding quaternary salts of N-oxides of the indicated bases. 12 quaternary salts were prepared.

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THE INTERACTION OF GLYCERIN, α, γ-DICHLOROHYDRIN WITH PCl₃, POCl₃, and PSCl₃

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Esters of phosphorous acid are converted by the action of alkyl halides to the isomeric esters of phosphonic acid [1]. M. I. Kabachnik and co-workers found tris-β-chloroethyl phosphite is converted to the isomeric penta-valent phosphorus compound without the addition of any catalyst. The chloroethyl group, which is present in the molecule, itself causes this conversion, and the boiling point of this ester under vacuum is sufficiently high that the isomerization goes to completion [2]. On the other hand, tris-β,β,β-trichloroethyl phosphite is not changed by heating for 5 hours at 160-165° [3]. In this regard, it was of interest to synthesize similar organophosphorus compounds containing chlorine in the β-position, and to study their chemical properties.

In 1945, Cook, Combie and Saunders published a paper [4] in which they reported the preparation of bis-β,β'-dichloroisopropylphosphorous acid[bis(1,3-dichloroisopropyl) hydrogen phosphite]-by the reaction of glycerin 1,3-dichlorohydrin with phosphorus trichloride in carbon tetrachloride. This product decomposed when distilled under a vacuum of 2 mm. Chlorination of the crude "bis-β,β'-dichloroisopropyl phosphite" gave bis-β,β'-dichloroisopropyl chlorophosphate[bis(1,3-dichloroisopropyl) chlorophosphate], which distilled with decomposition at 182-186° and 2 mm. It reacted with aniline to give bis(β,β'-dichloroisopropyl) anilinophosphate — fine, colorless needles with an m. p. of 81°. Jones and co-workers [5] obtained tris(β,β'-dichloroisopropyl) ortho-phosphate by the interaction of glycerin 1,3-dichlorohydrin and phosphoryl chloride in benzene solution in the presence of pyridine.

We found that glycerin 1,3-dichlorohydrin reacts with phosphorus trichloride in 1:1 ratio to give a mixture of products. The physical constants of these compounds are presented in the Table.
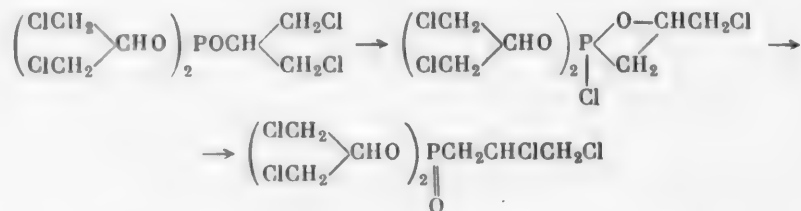
TABLE

Structural formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR	
				Calculated	Found
$\begin{array}{c}ClCH_2\\ClCH_2\end{array}$>CHOPCl₂	95—96° (12)	1.5118	1.5210	46.04	46.47
$\left(\begin{array}{c}ClCH_2\\ClCH_2\end{array}\right.$>CHO$\left.\right)_2$PCl	126—127 (0.2)	1.4891	1.5193	66.04	65.77
$\left(\begin{array}{c}ClCH_2\\ClCH_2\end{array}\right.$>CHO$\left.\right)_2$PCH₂CHClCH₂Cl $\overset{\parallel}{O}$	175—178 (0.07)	1.5010	1.5135	83.83	83.26

The first two products - the chlorides of bis β,β'-dichloroisopropyl- and β,β'-dichloroisopropylphosphorous acid[bis(1,3-dichloroisopropyl) chlorophosphite and 1,3-dichloroisopropyl dichlorophosphite]- are heavy, color-less liquids which fume in moist air. The third product is a very viscous, slightly mobile oil; it is colorless, and

has no odor. It does not react with cuprous chloride and phenyl azide (triazobenzene). Hydrolysis of this product with hydrochloric acid and treatment of the reaction mixture with barium carbonate gave barium 2,3-dichloro-n-propylphosphonate.

The conversion of trivalent to pentavalent phosphorus compounds probably proceeds according to a scheme similar to that proposed by M. I. Kabachnik for tris-(β-chloroethyl) phosphite [2].

$$\left(\begin{matrix}ClCH_2\\ClCH_2\end{matrix}\hspace{-0.2em}\rangle CHO\right)_2 POCH\hspace{-0.2em}\langle\begin{matrix}CH_2Cl\\CH_2Cl\end{matrix} \rightarrow \left(\begin{matrix}ClCH_2\\ClCH_2\end{matrix}\hspace{-0.2em}\rangle CHO\right)_2 \underset{\underset{Cl}{|}}{P}\hspace{-0.2em}\langle\begin{matrix}O-CHCH_2Cl\\CH_2\end{matrix} \rightarrow$$

$$\rightarrow \left(\begin{matrix}ClCH_2\\ClCH_2\end{matrix}\hspace{-0.2em}\rangle CHO\right)_2 \underset{\underset{O}{\|}}{P}CH_2CHClCH_2Cl$$

Hydrolysis of bis(1,3-dichloroisopropyl) chlorophosphite in ether solution with water, in the presence of pyridine to combine with the hydrogen chloride, gave the corresponding acid. This acid was a colorless, transparent liquid with almost no odor; it distilled without decomposition at 145-147° and 0.4 mm.

The interaction of glycerin 1,3-dichlorohydrin with phosphoryl chloride also forms a mixture of products, even at a reactant ratio of 1 to 1: the chloride of β,β'-dichloroisopropylphosphoric acid (1,3-dichloroisopropyl dichlorophosphate) $(ClCH_2)_2CHOPOCl_2$, the chloride of bis(β,β'-dichloroisopropyl)phosphoric acid [bis(1,3-dichloroisopropyl)chlorophosphate] [$ClCH_2)_2CHO]_2POCl$ and tris(1,3-dichloroisopropyl) phosphate $[(ClCH_2)_2CHO]_3$ PO.

This is the first preparation of 1,3-dichloroisopropyl dichlorophosphate (the physical constants are given under Experimental). Bis(1,3-dichloroisopropyl) chlorophosphate has been synthesized by Cook et al [4], who identified it by converting it to bis(1,3-dichloroisopropyl) anilinophosphate with an m. p. of 81°. The anilinophosphate prepared by us from bis(1,3-dichloroisopropyl) chlorophosphate had an m. p. of 80-81°. Tris(1,3-dichloroisopropyl) phosphate has previously been prepared by Jones and co-workers[5]. We were unable to purify this product.

Glycerin 1,3-dichlorohydrin reacts with thiophosphoryl chloride more difficultly than with phosphorus trichloride or phosphoryl chloride. Appreciable amounts of hydrogen chloride are evolved only when the reaction mixture is boiled. We were unable to obtain the individual reaction products.

EXPERIMENTAL

Interaction of glycerin 1,3-dichlorohydrin with phosphorus trichloride. 154.8 g of glycerin 1,3-dichlorohydrin was added dropwise to 164.4 g of phosphorus trichloride at 30°. The reaction mixture was held at this temperature for 1 hour, and was then distilled under vacuum. The following fractions were obtained: 1st, 93-100° at 12 mm, 88.1 g; 2nd, 120-140° at 0.3 mm, 80.0 g; 3rd, 170-185° at 0.3 mm, 28.4 g. All fractions were redistilled. From the first fraction was obtained 86.0 g (44.9% of the total amount) of 1,3-dichloroisopropyl dichlorophosphite. This is a colorless, mobile liquid with the odor of phosphorus trichloride; it fumes in moist air.

Found %: P 13.15, 13.26. $C_3H_5PCl_4$. Calculated % P 13.48.

During redistillation of the 2nd fraction, the bis(1,3-dichloroisopropyl) chlorophosphite was completely distilled at 126-127° and 0.2 mm. 79.1 g (40.1%) was obtained. The compound was a colorless, viscous liquid which fumed slightly in moist air.

Found %: P 9.85, 9.80. $C_6H_{10}O_2PCl_5$. Calculated %: P 9.63.

The redistillation of the third fraction proceeded very smoothly at 175-178° and 0.07 mm. This compound was a colorless, viscous oil, which was insoluble in water. The yield was 27.5 g (14.4%).

Found %: P 7.25, 7.05. $C_9H_{15}O_3PCl_6$. Calculated %: P 7.47.

Hydrolysis of bis(1,3-dichloroisopropyl) 2,3-dichloro-n-propylphosphonate. 3.2 g of the material and 5 ml of concentrated hydrochloric acid were sealed in a glass tube and heated at 150° for 10 hours. The hydrolysis

products were transferred to a distillation flask and evaporated under vacuum. The residue was dissolved in aqueous alcohol and treated with barium carbonate. A white, crystalline powder was formed, and carbon dioxide was evolved.

Found %: Ba 43.1, 42.9; P 9.15, 9.00. $C_3H_5O_3PBaCl_2$. Calculated %: Ba 42.0; P 9.44.

Hydrolysis of bis(1,3-dichloroisopropyl) chlorophosphite. 13.2 g of the chlorophosphite was placed in a three-neck flask fitted with a thermometer, a dropping funnel, a stirrer, and a reflux condenser, and 150 ml of absolute ethyl ether was added. The mixture was cooled to -5 to 0°, and, with stirring, a mixture of 0.73 g of water and 3.2 g of pyridine in 50 ml of ether was added dropwise. The precipitated pyridine hydrochloride was filtered, the ether was distilled, and the residue fractionated under vacuum. 7.5 g (61.5%) of product with a b.p. of 145-147° at 0.4 mm was obtained.

d_4^{20} 1.4865, $n^{20}D$ 1.5010, MR_D 60.32; calculated 60.41.

Bis(1,3-dichloroisopropyl) hydrogen phosphite is a colorless, viscous, odorless liquid.

Found %: P 10.25, 10.30. $C_6H_{11}O_3PCl_4$. Calculated %: P 10.20.

Interaction of glycerin 1,3-dichlorohydrin with phosphoryl chloride. 25.8 g of glycerin 1,3-dichlorohydrin was added dropwise to 30.6 g of phosphoryl chloride at 100°. The mixture was held for 2.5 hours at 130°, and was then distilled. The following fractions were obtained: 1st, 120-230° (12 mm), 18.1 g; 2nd, 120-130° (0.2 mm), 10.0 g; residue, 12.0 g.

Redistillation of the 1st fraction gave 1,3-dichloroisopropyl dichlorophosphite — a colorless, mobile liquid with the odor of phosphoryl chloride.

The b. p. was 122-124° at 12 mm; d_4^{20} 1.5800, $n^{20}D$ 1.4885, MR_D 44.86; calculated 44.96.

Found %: P 14.75, 14.80. $C_3H_5O_2PCl_3$. Calculated %: P 14.71.

Redistillation of the 2nd fraction gave a product with a b. p. of 180-182° at 2 mm. The distillation was accompanied by decomposition, and, therefore, the other constants of this compound were not determined. Reaction with aniline resulted in the formation of the anilinophosphate with an m. p. of 80-81°, which was identical to that prepared by Cook [4].

It was not possible to distill the tris(1,3-dichloroisopropyl) phosphate, owing to vigorous decomposition.

Interaction of glycerin 1,3-dichlorohydrin with thiophosphoryl chloride. 32.2 g of glycerin 1,3-dichlorohydrin was added dropwise, with stirring, to boiling thiophosphoryl chloride (42.5 g). Evolution of hydrogen chloride was very weak. After the addition of all of the glycerin 1,3-dichlorohydrin, the temperature was raised to 150° over the course of 1 hour. The reaction mixture was then distilled under vacuum. After the unreacted glycerin 1,3-dichlorohydrin and thiophosphoryl chloride had distilled at 50-67° (at 12 mm), the temperature rose rapidly to 120°, and then slowly increased to 220°. We were unable to separate the individual products. The products were light-yellow, viscous liquids with sharp, very disagreeable odors. Decomposition began toward the end of the distillation.

SUMMARY

1. The interaction of glycerin 1,3-dichlorohydrin with PCl_3 and $POCl_3$ at a reactant ratio of 1:1 proceeds with the formation of a mixture of organic phosphorus derivatives containing one, two, or three 1,3-dichloroisopropyl radicals.

2. The reaction becomes increasingly difficult in the order PCl_3, $POCl_3$, $PSCl_3$.

3. When heated during the course of distillation, tris(1,3-dichloroisopropyl) phosphite is converted to the isomeric bis(1,3-dichloroisopropyl) 2,3-dichloro-n-propylphosphonate.

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ON THE SO-CALLED "DI-β-NAPHTHYLACETAL"

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From the reaction of paraldehyde with β-naphthol in a mixture of acetic and hydrochloric acids, Claisen [1] obtained a substance with an m. p. of 200-201°, to which he ascribed the structure of acetaldehyde β-naphthyl acetal. "Di-β-naphthylacetal" was later prepared by Wenzke and Nieuwland [2] by the interaction of acetylene with β-naphthol. Since this substance has repeatedly been described in the literature as "di-β-naphthylacetal" and since it has been considered an intermediate product in certain reactions [1, 3], we have carried out a more detailed study of this compound.

The formation of the di-β-naphthyl acetal from acetaldehyde would appear to be improbable, because formaldehyde does not form the analogous acetal under similar conditions. The latter can be prepared only by lengthy heating of β-naphthol with methylene iodide in a sealed tube in the presence of a base [4]. We have been able to establish that, under the same conditions, crotonaldehyde gives the same substance as acetaldehyde, and by careful analysis it was found that the formation of the substance with an m. p. of 200-201° from acetaldehyde and β-naphthol proceeds according to the equation $2CH_3CHO + 2C_{10}H_7OH \rightarrow C_{24}H_{20}O_2 + 2H_2O$.

This substance forms derivatives - a monobenzoyl derivative (m. p. 178°) by heating with benzoyl chloride and a monoacetyl derivative (m. p. 154-155°) by refluxing with acetic anhydride; it contains 1 active hydrogen atom; acidification of the product of its interaction with methylmagnesium iodide precipitates the original substance unchanged. Hydrolysis of the acetyl derivative also leads to the original substance.

On distillation, the substance decomposes to β-naphthol and a white, crystalline substance with an m. p. of 90-92°, which, according to the analytical data and molecular-weight determination, corresponds to the formula $C_{14}H_{14}O$. Thus, the decomposition of "di-β-naphthylacetal" proceeds according to $C_{24}H_{20}O_2 \rightarrow C_{14}H_{14}O + C_{10}H_7OH$.

These facts leave no doubt that the so-called "di-β-naphthylacetal" of Claisen has a structure which is totally different than that which has formerly been ascribed to it.

Dianin [5] has reported on the condensation of mesityl oxide with phenol, which, as established by Baker and co-workers [6] results in the formation of 4-p-hydroxyphenyl-2,2,4-trimethylchroman, and this compound, in turn, decomposes on heating to phenol and 2,2,4-trimethylchromene; on the basis of this work, it can be assumed that in the case of the condensation of β-naphthol with acetaldehyde, crotonaldehyde is initially formed, that the reaction subsequently follows the same course with the formation of 4-(1-2-hydroxynaphthyl) - 2- methyl-5,6-benzochroman (I), and that thermal decomposition would lead to the chromene (II) and β-naphthol.

(I)   (II)
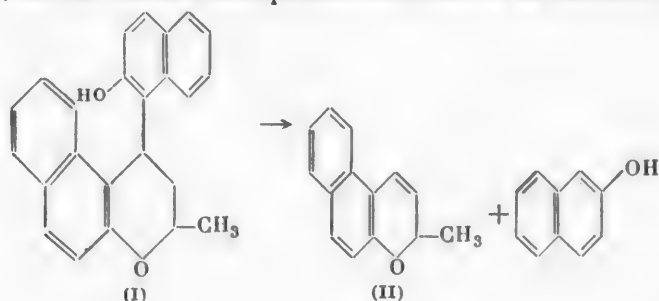
Considering the analytical data and the fact that chromenes of the type of (II) tend to disproportionate at elevated temperatures with the formation of polymer and a chroman [7], the structure of 2-methyl-5,6-benzo-chroman (III) may be proposed for the substance with an m. p. of 90-92°.

(III)
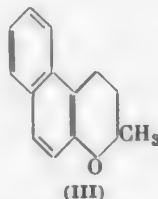
Compound (III) has been described in the literature [8]. It also has an m. p. of 90-91°. Our substance with an m. p. of 90-92° does not react with bromine solution at room temperature, and this makes it probable that formula (II) is correct.

It is characteristic that the so-called "di-β-naphthylacetal", like Dianin's compound, does not give a color with ferric chloride, dissolves in bases with considerable difficulty, and gives a yellow-green color with concentrated sulfuric acid.

EXPERIMENTAL

Preparation of "di-β-naphthylacetal" by Claisen's method [9]. 7 g of β-naphthol and 3 g of paraldehyde were dissolved in 15 ml of glacial acetic acid, and to the solution was added 1 ml of hydrochloric acid (d 1.19). The mixture was heated on a water bath, and an oil layer separated. The mixture was cooled, and the resulting crystals, after recrystallization from chloroform, melted at 200-201°. The substance was soluble only in hot aqueous-alcoholic bases, and it did not give a color with an alcoholic solution of ferric chloride.

Found %: C 84.92; H 5.70. M 344.4, 348.2 (ebullioscopic, in acetone); act. H 1.07 (in isoamyl ether), 1.08 (in pyridine). $C_{24}H_{19}O(OH)$. Calculated %: C 84.70; H 5.88. M 340; act. H 1.

The acetyl derivative was prepared by refluxing with acetic anhydride. 58.4 g of acetylation product was obtained from 80 g of "di-β-naphthylacetal." After two recrystallizations from glacial acetic acid, the substance melted at 154-155°.

Found %: C 81.49; H 6.00. M 378.1 (ebullioscopic, in acetone). $C_{26}H_{22}O_3$. Calculated %: C 81.68; H 5.76. M 382.

When refluxed with an alcoholic solution of sodium hydroxide, the acetyl derivative was hydrolyzed to the original product with an m. p. of 200-201°.

The benzoyl derivative, m. p. 178°, was prepared by heating "di-β-naphthylacetal" with benzoyl chloride.

Found %: C 83.62; H 5.89. M 436 (ebullioscopic, in acetone). $C_{31}H_{24}O_3$. Calculated %: C 83.77; H 5.41. M 444.

A white precipitate of the Mg salt was formed when a solution of methylmagnesium iodide was added to a dry ether solution of "di-β-naphthylacetal"; after filtration and treatment of the salt with dilute hydrochloric acid, the original substance with an m. p. of 200-201° was obtained in almost quantitative yield.

Reaction of β-naphthol with crotonaldehyde. 3 g of crotonaldehyde (b. p. 104-106°, p-nitrophenylhydrazone m. p. 183-185°), 7 g of β-naphthol, 15 ml of glacial acetic acid, and 1 ml of hydrochloric acid (d 1.19) were heated on a water bath. The oil which separated was purified as indicated above. After recrystallization from chloroform, the white crystals melted at 200°. A mixture with the previously prepared "di-β-naphthylacetal" showed no depression of the melting point.

Thermal decomposition of "di-β-naphthylacetal." 30 g of the substance was melted in a retort, which was then heated strongly. A rapidly crystallizing oil distilled at 310-325°. The weight was 24.3 g. The distillate was treated with 20% sodium hydroxide and then with ether. The alkaline layer was acidified. The crystals of β-naphthol were suction-filtered and dried. The weight was 13.3 g; m. p. 117°. The acetyl derivative had

an m. p. of 68-69°; a mixture with a known sample of the acetyl derivative melted without depression of the melting point. Distillation of the solvent from the ether layer gave a partially crystallized oil. The weight was 7.8 g. The oil was washed with alcohol. The white powder was recrystallized from alcohol. The m. p. was 90-92°. The weight was 1.9 g.

Found %: C 84.47; H 7.22. M 193.4 (ebullioscopic, in acetone). $C_{14}H_{12}O$. Calculated %: C 85.70; H 6.12. M 196. $C_{14}H_{14}O$. Calculated %: C 84.84; H 7.07. M 198.

SUMMARY

1. It was shown that the product of the condensation of β-naphthol with paraldehyde is not the di-β-naphthyl acetal.

2. The reactions and analysis of the condensation product make it possible to describe the compound as 4-[1-(2-hydroxynaphthyl)]-2-methyl-5,6-benzochroman.

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C-CHLORO-P,P-DIMETHOXY- AND C-CHLORO-P,P-DIAROXY-ISOPHOSPHAZOACYLS

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Trichloroisophosphazoacyls have recently been prepared by the action of phosphorus pentachloride on acylamidophosphoric dichlorides [1] according to the scheme

$$RCONHPOCl_2 + PCl_5 \longrightarrow HCl + POCl_3 + RCCl{=}NPOCl_2.$$

It was, therefore, of interest to discover whether this reaction could be extended to the diesters of acyl-amidophosphoric acids so as to obtain C-chloro-P,P-dialkoxy- and C-chloro-P,P-diaroxyisophosphazoacyls (I) according to

$$RCONHPO(OR')_2 + PCl_5 \longrightarrow HCl + POCl_3 + RCCl{=}NPO(OR')_2 \qquad \text{(II)}$$
$$\text{(I)}$$
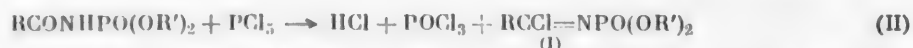
In their chemical nature, the C-chloro-P,P-diaroxyisophosphazoacyls are acid chlorides of diesters of imidophosphoric acids (see reference [2] for nomenclature), and they therefore exhibit, on the one hand, the properties of imidic acids and the properties of esters of amidophosphoric acids, on the other.

The preparation of (I) is of interest, since similar compounds are unknown, and it is clearly possible to prepare from them a series of new types of phosphoric acid derivatives.

The experiments showed that reaction (II) takes place with considerably greater ease than does the reaction of phosphorus pentachloride with acylamidophosphoric dichlorides. Thus, for example, when equivalent amounts of phosphorus pentachloride and the dimethyl ester of an acylamidophosphoric acid are mixed, the reaction proceeds quite violently even at room temperature. The diphenyl esters of acylamidophosphoric acids react with phosphorus pentachloride with somewhat greater difficulty, but the di(p-nitrophenyl) and di(p-chloro-phenyl) esters react with phosphorus pentachloride under approximately the same conditions as the acylamido-phosphoric dichlorides. During the reaction, 80-90% of the hydrogen chloride and about 90% of the theoretical amount of phosphoryl chloride are evolved, and these are collected and determined by the usual methods. Ben-zene and chlorobenzene can be used as solvents for the reactions of the dimethyl esters of acylamidophosphoric acids with phosphorus pentachloride; only chlorobenzene can be used for the remaining diesters. The reactions also proceed readily without a solvent, but the products are less pure and more difficult to crystallize, probably owing to local overheating. The reactions proceed much more smoothly in chlorobenzene, and the distillation of the phosphoryl chloride is much easier in the presence of chlorobenzene. Removal of the phosphoryl chloride by washing with various solvents is attended by considerable loss of (I).

C-Chloro-P,P-dimethoxyphosphazoacyls are viscous, oily liquids or low-melting solids. It is very diffi-cult to isolate them in the crystalline state, since when they are removed from the reaction vessel, they deli-quesce very rapidly, reacting with atmospheric moisture. C-Chloro-P,P-diaroxyisophosphazoacyls are consider-ably more stable toward atmospheric moisture, and are readily isolated as well-formed crystals with sharp melt-ing points.

All compounds of type (I) are very reactive; they readily react with water, sodium alcoholates and pheno-lates, amines, and other compounds containing active hydrogen or metal atoms. They have a characteristic odor of benzonitrile. In the absence of moisture, they can be stored without change for quite long periods of time,

TABLE

C-Chloro-P,P-dimethoxy- and C-Chloro-P,P-diaroxyisophosphazoacyls, RCCl = NPO(OR')₂

R	R'	Yield(in %)	Melting point	Crystal form and crystallization solvent	Empirical formula	Found equiv. after hydrolysis*
C₆H₅	CH₃	100.0	—	Viscous liquid	$C_9H_{11}O_3NP\ Cl$	2.05
P-NO₂C₆H₄	CH₃	100.0	107—110°	Coarse "soft" prisms	$C_9H_{10}O_5N_2PCl$	2.01
m-NO₂C₆H₄	CH₃	89.6	20—25	Long "soft" prisms	$C_9H_{10}O_5N_2PCl$	1.97
3,5-(NO₂)₂C₆H₃	CH₃	95.5	125—127	Coarse prisms	$C_9H_9O_7N_3PCl$	2.01
p-ClC₆H₄	CH₃	99.5	—	Liquid	$C_9H_{10}O_3NPCl_2$	1.97
C₆H₅	C₆H₅	42.5 ****	74—76	Coarse prisms, petroleum ether	$C_{19}H_{15}O_3NPCl$ **	2.01
P-NO₂C₆H₄	C₆H₅	83.5 ******	87—89	Prisms, petroleum ether	$C_{10}H_{14}O_5N_2PCl$ ***	2.02
m-NO₂C₆H₄	C₆H₅	81.7	127—129	Rhombic plates, mixture of benzene and petroleum ether	$C_9H_{14}O_5N_2PCl$	2.02
3,5-(NO₂)₂C₆H₃	C₆H₅	61.6	115—118	Prisms, mixture of benzene and petroleum ether	$C_{10}H_{13}O_7N_3PCl$	1.99
P-ClC₆H₄	C₆H₅	100.0	55—57	Prisms, petroleum ether	$C_{19}H_{14}O_3NPCl_2$	2.00
C₆H₅	p-ClC₆H₄	35.4	69—71	Coarse prisms, benzene	$C_{19}H_{13}O_3NPCl_2$ ******	2.03
p-NO₂C₆H₄	p-ClC₆H₄	92.3	150—152	Prism agglomerates, benzene	$C_{19}H_{12}O_5N_2PCl_3$	1.98
p-ClC₆H₄	p-ClC₆H₄	69.7	109—111	Prisms, Benzene	$C_{19}H_{12}O_3NPCl_4$	2.06
C₆H₅	p-NO₂C₆H₄	95.7	157—160	Prisms, chlorobenzene	$C_{19}H_{13}O_7N_3PCl$	2.01
p-NO₂C₆H₄	p-NO₂C₆H₄	80.0	161—163	Prisms, chlorobenzene	$C_{19}H_{12}O_9N_4PCl$	1.98
p-ClC₆H₄	p-NO₂C₆H₄	89.0	137—139	Acigular agglomerates, benzene	$C_{19}H_{12}O_7N_3PCl_2$	2.01

* Calculated equiv. after hydrolysis, 2.00.
** Found %: Cl 10.0; N 3.90. Calculated %: Cl 9.54; N 3.77.
*** Found. %: Cl 9.15; N 6.91. Calculated, %: Cl 8.51; N 6.72.
**** Including material recovered from the mother liquor, the yield was about 83%.
***** The substance hydrolyzes very readily, and, on standing in air for a short time, it is completely converted to the corresponding diester.
****** Including material recovered from the mother liquor, the yield was about 95%.

and when agitated with water or when allowed to stand in air, they are quantitatively converted to the original acylamidophosphoric diesters; this is reliable proof of their structure. They titrate to a phenolphthalein end point with 2 equivalents of base in aqueous-alcoholic solution. On thermal decomposition, (I) gives almost quantitative yields of the nitrile and the corresponding esters of phosphoric acid chlorides according to the scheme

$$RCCl=NPO(OR')_2 \rightarrow RCN + ClPO(OR')_2.$$

The reaction takes place in 10-15 minutes at 250-300° and 20-22 mm. The nitriles were identified by boiling or melting point; the acid chlorides were converted to the amides and identified by melting point.

EXPERIMENTAL

C-Chloro-P,P-dimethoxyisophosphazoacyls. 0.01 mole of the dimethyl ester of the acylamidophosphoric acid was mixed with 0.01 mole of phosphorus pentachloride and 10-15 ml of dry benzene or chlorobenzene. The reaction began at room temperature and proceeded rather vigorously. When the evolution of hydrogen chloride began to slow down, the reaction mixture was heated on an oil bath for 5-10 minutes at 60-70°, and the phosphoryl chloride and solvent were distilled under vacuum. 80-90% of the hydrogen chloride was liberated during the reaction, and this was collected and determined in the usual manner. The residue contained the C-chloro-P,P-dimethoxyisophosphazoacyl as a viscous, transparent liquid or as a "soft" crystalline material, which, when removed from the reaction vessel, lost its crystalline form and rapidly deliquesced. All of the C-chloro-P,P-dimethoxyisophosphazoacyls were readily soluble in acetone and benzene, and more difficultly soluble in ether, petroleum ether, carbon tetrachloride, and chlorobenzene. The compounds prepared are described in the table.

C-Chloro-P,P-diphenoxyisophosphazoacyls. 0.01 mole of the diphenyl ester of the acylamidophosphoric acid was mixed with 0.01 mole of phosphorus pentachloride and 15-20 ml of chlorobenzene, and the mixture was heated on an oil bath at 100-105° until the evolution of hydrogen chloride ceased, which required 10-15 minutes. The phosphoryl chloride and the chlorobenzene were distilled under vacuum. The residue contained the C-chloro-P,P-diphenoxyisophosphazoacyl as a dense, crystalline precipitate or as a liquid which rapidly crystallized when ground with a glass rod in the presence of 2-3 ml of petroleum ether. C-Chloro-P,P-diphenoxyisophosphazoacyls may be crystallized from benzene, petroleum ether, or their mixtures. All of these compounds are readily soluble in acetone and benzene, and more difficultly soluble in chlorobenzene, petroleum ether, ether, and carbon tetrachloride (see table).

C-Chloro-P,P-di(p-chlorophenoxy)isophosphazoacyls. 0.01 mole of the di(p-chlorophenyl) ester of the acylamidophosphoric acid, 0.01 mole of phosphorus pentachloride, and 15-20 ml of chlorobenzene was heated on an oil bath at 110-115° until the evolution of hydrogen chloride completely ceased, which required 20-25 minutes. The phosphoryl chloride and part of the chlorobenzene were distilled under vacuum. 5-6 ml of petroleum ether was added to the remaining solution, and the mixture was allowed to stand for 1-3 hours. The crystallized product (usually coarse, well-formed prisms) was suction-filtered, washed with petroleum ether (2 ml) and with ether (3 ml), and dried. The C-chloro-P,P-di(p-chlorophenoxy)phosphazoacyls prepared in this manner were practically pure, and did not require recrystallization; when necessary, they can be crystallized from benzene or chlorobenzene. The yields of products were 80-90%. All of the C-chloro-P,P-di(p-chlorophenoxy)isophosphazoacyls were quite readily soluble in benzene and acetone, somewhat less soluble in chlorobenzene, and difficultly soluble in petroleum ether, ether, and carbon tetrachloride (see table).

C-Chloro-P,P-di(p-nitrophenoxy)isophosphazoacyls. 0.01 mole of the di p-nitrophenyl) ester of the acylamidophosphoric acid, 0.01 mole of phosphorus pentachloride, and 15-20 ml of chlorobenzene were heated on an oil bath at 110-120° until the evolution of hydrogen chloride ceased completely, which required 30-40 minutes. About 90% of the hydrogen chloride was liberated during this period, and this was collected and determined in the usual manner. The phosphoryl chloride and part (approximately half) of the chlorobenzene were distilled under vacuum. On cooling of the solution, the C-chloro-P,P-di(p-nitrophenoxy)isophosphazoacyl crystallized as coarse, well-formed prisms, which were filtered, washed with petroleum ether (3 ml) and with ether (3 ml), and dried. The products were quite pure, and did not require recrystallization; they can be recrystallized from benzene or chlorobenzene. The yields (including material recovered from the mother liquors) were almost quantitative. C-Chloro-P,P-di(p-phenoxy)isophosphazoacyls are difficultly soluble in benzene, acetone, and chlorobenzene and still more difficultly soluble in petroleum ether, ether, and carbon tetrachloride (see table).

Thermal decomposition of C-chloro-P,P-diaroxyisophosphazoacyls. 0.02 mole of C-chloro-P,P-diphenoxyisophosphazobenzoyl was placed in a 25-ml Claisen flask fitted with a capillary and thermometer and gradually heated under vacuum (20 mm) on an oil bath. Decomposition began at a bath temperature of 230-240° and ended within 8-10 minutes. About 90% (1.85 g) of the benzonitrile and about 8-9% of an intermediate fraction (0.16 g) distilled during this time. The remaining material (96.6%, 5.2 g) was treated with concentrated aqueous ammonia, and the resulting crystals of the diphenyl ester of amidophosphoric acid were recrystallized from alcohol; the m. p. was 144-146°. which agrees with the literature value [3]. The decomposition of C-chloro-P,P-diphenoxyisophosphazo-m-nitrobenzoyl was carried out in the same manner. The decomposition temperature was 230-240°. A 91.3% yield of n-nitrobenzonitrile and a 95.2% yield of the diphenyl ester of chlorophosphoric acid were obtained. C-Chloro-P,P-di(p-nitrophenoxy)isophosphazobenzoyl was decomposed at 250-260° (21 mm). The yields of benzonitrile and di(p-nitrophenyl) ester of chlorophosphoric acid were 97.4% and 96.4%, respectively. The ester was treated with a 2 N solution of sodium hydroxide. and the solution was acidified with hydrochloric acid to precipitate di(p-nitrophenyl) phosphate; the m. p., 174-176°, agrees with the literature value [4]. Other C-chloro-P,P-dimethoxy- and -diaroxyisophosphazoacyls were decomposed in a similar manner.

Hydrolysis of C-chloro-P,P-dimethoxy- and C-chloro-P,P-diaroxyisophosphazoacyls. 0.01 mole of the compound was mixed with 10 ml of water, and the mixture was allowed to stand at room temperature. Hydrolysis was complete after 2-2.5 hours. The diesters of acylaminophosphoric acids were suction-filtered, washed with water, and dried in air. The yields were 96-99%;identification of the products was by mixed melting point.

SUMMARY

1. C-Chloro-P,P-dimethoxy- and C-chloro-P,P-diaroxyisophosphazoacyls were prepared by the action of phosphorus pentachloride on diesters of acylamidophosphoric acids.

2. Thermal decomposition of the C-chloro-P,P-dimethoxy- and C-chloro-P,P-diaroxyisophosphazoacyls gave the corresponding nitriles and dimethyl and diaryl esters of chlorophosphoric acid.

3. Hydrolysis of the C-chloro-P,P-dimethoxy- and C-chloro-P,P-diaroxyisophosphazoacyls gave the corresponding diesters of acylamidophosphoric acids.

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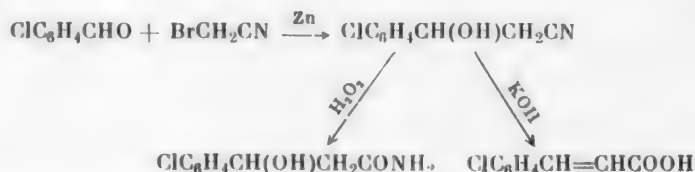*Original Russian pagination. See C. B. translation.

THE REFORMATSKY REACTION WITH α-HALONITRILES

II. THE CONDENSATION OF CHLOROBENZALDEHYDES WITH BROMOACETONITRILE

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In a previous communication [1], we described the condensation of benzaldehyde with bromoacetonitrile under Reformatsky reaction conditions; the reaction proceeds with the formation of β-hydroxy-β-phenylpropionitrile. In a continuation of this work, we have studied the condensation of o-, m-, and p-chlorobenzaldehydes with bromoacetonitrile under the usual conditions for Reformatsky reactions. As in the case of unsubstituted benzaldehyde, we obtained the previously undescribed β-hydroxy-β-chlorophenylpropionitriles. The nitriles were characterized by elemental analysis, by conversion through Radziszewski's reaction [2] to the corresponding, also previously undescribed, hydroxyamides, and by hydrolysis to the known trans-o-, m-, and p-chlorocinnamic acids.

$$ClC_6H_4CHO + BrCH_2CN \xrightarrow{Zn} ClC_6H_4CH(OH)CH_2CN$$

$$\overset{H_2O_2}{\swarrow} \qquad \overset{KOH}{\searrow}$$

$$ClC_6H_4CH(OH)CH_2CONH_2 \qquad ClC_6H_4CH=CHCOOH$$

It should be pointed out that the introduction of a chlorine atom into the 4-position of benzaldehyde somewhat increases the yield of hydroxynitrile as compared to the yield obtained with the unsubstituted aldehyde [1] (53.4% instead of 48.2%), while the introduction of chlorine into the 2-position and, particularly, into the 3-position reduces the yield of hydroxynitrile (43.0 and 27.6%, respectively). However, when the reaction is carried out in the presence of mercuric chloride [3], the yield of β-hydroxy-β-(3-chlorophenyl)propionitrile is increased to 50.7%.

EXPERIMENTAL

β-Hydroxy-β-(4-chlorophenyl)propionitrile. 6 g of bromoacetonitrile was added, over a 15-minute period to a boiling mixture of 7 g of p-chlorobenzaldehyde, prepared by the method of reference [4], 4.5 g of activated zinc dust, 8 ml of dry benzene, and 2 ml of dry ether. The mixture was stirred and refluxed for an additional 45 minutes. 20 ml of dry benzene was added 10 minutes after the beginning of the addition of nitrile, since the mixture had thickened. The mixture was cooled to room temperature and stirred for 1 hour with 35 ml of 10% sulfuric acid (ice cooling). The very small amount of precipitate was filtered, and the benzene layer was separated and washed with a 5% solution of sulfuric acid, then with a 5% soda solution, and finally with water. The water layer and the acid wash water were extracted with benzene. The washed extract was added to the main portion. The benzene and ether were distilled, and the residue was distilled under vacuum in a stream of nitrogen. The following distillate fractions were collected: 75-80° (5 mm), 0.8 g (unchanged aldehyde) and 178-180° (5 mm), 4.85 g (53.4%) β-hydroxy-β-(4-chlorophenyl)propionitrile — a light-yellow, viscous liquid which soon crystallized. The m. p. was 49.5-50.5°. It was readily soluble in methanol. Two recrystallizations from 200 and 250 ml of CCl_4 gave 3.2 g of colorless crystals with an m. p. of 53-53.5°.

Found %: C 59.63; H 4.61; N 7.73; Cl 19.41. C_9H_8NCl. Calculated %: C 59.51; H 4.44; N 7.71; Cl 19.52.

β-Hydroxy-β-(4-chlorophenyl)propionamide. 1 g of β-hydroxy-β-(4-chlorophenyl)propionitrile, 2 ml of water, 4 ml of 30% H_2O_2, 0.5 ml of 1 N KOH, and 1 ml of methanol were vigorously stirred for 1.5 hours at 40-60°. The nitrile completely dissolved during this time. White, lamellar crystals (0.9 g) precipitated as the reaction mixture was cooled to room temperature; the crystals were readily soluble in methanol and hot water and sparingly soluble in benzene, CCl_4, and cold water. Recrystallization from 6 ml of water gave 0.5 g (45.5%) of β-hydroxy-β-(4-chlorophenyl)propionitrile with an m. p. of 130-131.5°.

Found %: C 54.09, 54.06; H 4.85, 4.91; N 7.10, 6.92. $C_9H_{10}O_2Cl$. Calculated %: C 54.14; H 5.049; N 7.016.

Trans-4-chlorocinnamic acid. 0.6 g of β-hydroxy-β-(4-chlorophenyl)propionitrile was refluxed for 4 hours with 30 ml of 2 N KOH diluted with 100 ml of water; the mixture was then filtered from the very small amount of solid, and acidified with dilute (1:1) hydrochloric acid. The resulting precipitate was filtered and washed with water. The acid melted at 246.5-247° (literature value [5]: 247°).

β-Hydroxy-β-(2-chlorophenyl)propionitrile. The nitrile was prepared from 7 g of 2-chlorobenzaldehyde (prepared by the method of reference [6]) by refluxing the reaction mixture for 1 hour without the addition of benzene. Distillation gave the following fractions: 60-65° (2 mm), 1.55 g, unchanged aldehyde, and 153-156° (2 mm), 3.9 g (43%), β-hydroxy-β-(2-chlorophenyl)propionitrile — a light-orange, viscous liquid. On standing for 20 days at 0°, the liquid crystallized. Recrystallization from 60 ml of CCl_4 gave 2.3 g of crystals, thin leaves with a pearly luster. M. p. 61-62°.

Found %: C 59.59; H 4.62; Cl 19.48. C_9H_8NCl. Calculated %: C 59.51; H 4.44; Cl 19.52.

β-Hydroxy-β-(2-chlorophenyl)propionamide was prepared from 0.5 g of the nitrile with a 30-minute refluxing. Recrystallization from 200 ml of water gave 0.4 g (72.5%) of needles with an m. p. of 192.5-193°.

Found %: C 54.23; H 5.01; Cl 17.72. $C_9H_{10}O_2N_3Cl$. Calculated %: C 54.14; H 5.049; Cl 17.76.

Trans-2-chlorocinnamic acid was prepared in a manner similar to that used in the preparation of the 4-chloro isomer. Needles with an m. p. of 209.5° (literature value [5], 211°) were obtained by recrystallization from methanol.

β-Hydroxy-β-(3-chlorophenyl)propionitrile. a) The nitrile was prepared from 7 g of 3-chlorobenzaldehyde, prepared by the method of reference [7], by refluxing the reaction mixture for 3 hours without the addition of benzene. The following fractions were collected during the distillation: 60-120° (1 mm), 0.7 g, unchanged aldehyde containing some bromoacetonitrile, and 152-156° (1 mm), 2.5 g (27.6%), β-hydroxy-β-(3-chlorophenyl)propionitrile.

b) The reaction was carried out in a similar manner but in the presence of 0.1 g of mercuric chloride. The following fractions were collected during the distillation: 60-120° (1 mm), 1.4 g, unchanged aldehyde containing some bromoacetonitrile, and 152-156° (1 mm), 4.6 g (50.7%), β-hydroxy-β-(3-chlorophenyl)propionitrile — a colorless, viscous liquid.

Found %: C 59.70; H 4.57; N 7.73; Cl 19.64. C_9H_8NCl. Calculated %: C 59.51; H 4.44; N 7.71; Cl 19.52.

β-Hydroxy-β-(3-chlorophenyl)propionamide, was obtained from 0.5 g of the nitrile. The amide crystallized after standing for 2 days, and two recrystallizations from alcohol gave 0.25 g (45.5%) of a substance with an m. p. of 134-135°.

Found %: C 54.51; H 5.00; N 7.22. $C_9H_{10}O_2NCl$. Calculated %: C 54.14; H 5.049; N 7.016.

Trans-3-chlorocinnamic acid was prepared from 0.4 g of β-hydroxy-β-(3-chlorophenyl)propionitrile by the method described for the preparation of the 4-chloro isomer; 0.15 g of the acid was obtained. Recrystallization from 2 ml of methanol gave 3-chlorocinnamic acid with an m. p. of 164° (literature value [5], 165°).

Found %: C 59.21; H 3.88. $C_9H_7O_2Cl$. Calculated %: C 59.2; H 3.84.

SUMMARY

1. β-Hydroxy-β-(o-, m, and p-chlorophenyl)propionitriles were prepared by condensation of o-, m-, and p-chlorobenzaldehydes with bromoacetonitrile under Reformatsky conditions, and from them were obtained

the corresponding β-hydroxy-β-(chlorophenyl)propionamides; all of these compounds were characterized.

2. It was found that the addition of mercuric chloride considerably increases the yield of β-hydroxy-β-(3-chlorophenyl)propionitrile.

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INVESTIGATIONS IN THE FIELD OF ORGANOCYCLOSILOXANES
V. ALKYLCYCLOTETRASILOXANES WITH FUNCTIONAL GROUPS

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We have previously described certain organocyclosiloxanes with functional groups (H, Cl) at the silicon atoms [1, 2]. Below we describe the preparation of alkylcyclosiloxanes with functional groups at the silicons by cohydrolysis of dimethyldichlorosilane with methyldichlorosilane or ethyldichlorosilane in a molar ratio of 1:0.5. The use of these monomers in the cohydrolysis reaction results in the formation of cyclic compound rings composed of with mixed units. The presence of a hydrogen atom attached to a ring silicon makes possible the further preparation of derivatives.
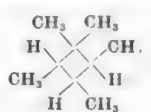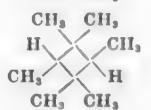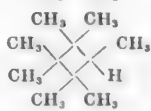
At the conclusion of the cohydrolysis the cyclic compounds were distilled from the linear compounds and then fractionated. The remaining, undistillable linear and higher cyclic compounds were thermally rearranged at 300-360°, and the rearrangement products were subsequently fractionated. It was found that both of these methods give cyclic compounds with rings composed of mixed units.

The properties of the tetramers are presented in Table 1.

Approximately the same amount of cyclic tetramers is formed during thermal rearrangement as during hydrolysis (Table 2).

TABLE 1

Methylcyclosiloxanes Formed by Cohydrolysis and by Thermal Rearrangement

Cyclosiloxane	Formula *	Temperature		n_D^{20}	d_4^{20}
		B.p. (press. in mm)	M.p.(± 1°)		
1,1,3,5,7-Pentamethyl-cyclotetrasiloxane	CH_3 CH_3 H CH_3 CH_3 H H CH_3	69° (50), 50.5 (20)	−52°	1.3913	0.9718
1,1,3,5,5,7-Hexamethyl-cyclotetrasiloxane	CH_3 CH_3 H CH_3 CH_3 H CH_3 CH_3	58.5—59 (20), 77.5 (50)	−40	1.3935	0.9674
Heptamethylcyclotetra-siloxane	CH_3 CH_3 CH_3 CH_3 CH_3 H CH_3 CH_3	84.5 (50), 66 (20)	−27	1.3965	0.9583

* The square denotes the $(Si-O)_n$ ring.

Almost half of the mixture of cyclic compounds consisted of rings higher than tetramers (these were not separated). This is explained by the effect of the methyldichlorosilane, which tends considerably toward the formation of linear polymers and, apparently, larger rings. Of the 1860 g of methylchlorosilanes cohydrolyzed, a total of 1065 g was recovered as cohydrolysis products; the loss during thermal rearrangement was 43 g.
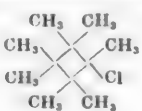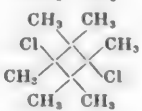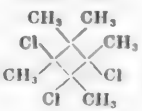
TABLE 2

Amount of Cyclic Tetramers Separated from the Products of the Hydrolysis of $(CH_3)_2SiCl_2$ + + CH_3SiHCl_2 (1:0.5)

Cyclosiloxane	From 435 g of cyclics from hydrolysis		From 585 g of cyclics from rearrangement		Total from 1020 g	
	g	%	g	%	g	%
Hexamethylcyclotrisiloxane + tetramethyl-cyclotetrasiloxane	19	4.4	34	5.8	53	5.2
Pentamethylcyclotetrasiloxane	18	4.2	19	3.3	37	3.6
Hexamethylcyclotetrasiloxane	50	11.5	64	11.0	114	11.2
Pentamethylcyclotetrasiloxane	90	20.6	58	9.9	148	14.5
Octamethylcyclotetrasiloxane	86	19.8	96	16.4	182	17.9
Total	263	60.5	271	46.4	534	52.4

TABLE 3

Methylchlorocyclosiloxanes with Mixed Units

Methylchlorocyclosiloxane	Formula	Temperature		d_4^{20}
		B.p. (press. in mm)	M.p. ($\pm 1°$)	
Pentamethylchlorocyclo-tetrasiloxane	CH_3 CH_3 / CH_3 CH_3 / CH_3 Cl / CH_3 CH_3	85.5—86.5° (20)	6°	1.0231
Hexamethyl-1,5-dichloro-cyclotetrasiloxane	CH_3 CH_3 / Cl CH_3 / CH_3 Cl / CH_3 CH_3	93—95 (20)	24	1.1251
Pentamethyl-1,3,5-tri-chlorocyclotetrasiloxane	CH_3 CH_3 / Cl CH_3 / CH_3 Cl / Cl CH_3	105—106 (20)	36	—

The H(—Si)contents of the kettle residues from the distillations of the hydrolysis products and the thermally rearranged products were 0.63 and 0.84%. The average of these two values corresponds almost exactly to the value (0.75%) calculated for the unit $(CH_3)_2SiOSiCH_3H$.

It can be concluded from these experiments that cohydrolysis of these monomers proceeds quite completely and uniformly with the formation both of cyclic and of linear compounds.

The compounds shown in Table 3 were obtained by chlorination of the cyclic tetramers with rings composed of mixed units.

Chlorinated tetramers with 2, 3, and 4 chlorine atoms are crystalline substances at 20°. The boiling and melting points of the chlorinated tetramers vary directly with the change in the number of chlorine atoms.

Cohydrolysis of dimethyldichlorosilane and ethyldichlorosilane in 1:3 molar ratio followed by thermal rearrangement of the hydrolysis products also led to the formation of two cyclic compounds containing mixed units. These compounds and their chlorinated derivatives are presented in Table 4.

TABLE 4

Methylethylcyclosiloxanes

| Cyclosiloxane | Formula | Temperature | | n_D^{20} | d_4^{20} | Yield (in %) |
		B.p. (press. in mm)	M.p.			
1,1,3,3,5,5-Hexamethyl-7-ethylcyclotetrasiloxane	CH₃ CH₃ / CH₃ C₂H₅ / CH₃ H / CH₃ CH₃	80° (20)	−36°	1.4000	0.9574	9.8
1,1,5,5-Tetramethyl-3,7-diethylcyclotetrasiloxane	CH₃ CH₃ / H C₂H₅ / C₂H₅ H / CH₃ CH₃	88 (20)	−93	1.4045	0.9644	10.0
1-Ethyl-1-chlorohexamethylcyclotetrasiloxane	CH₃ CH₃ / CH₃ C₂H₅ / CH₃ Cl / CH₃ CH₃	135—138 (20)	−38	—	1.1730	62
1,5-Diethyl-1,5-dichlorotetramethylcyclosiloxane	CH₃ CH₃ / Cl C₂H₅ / C₂H₅ Cl / CH₃ CH₃	126—129 (1)	−48	—	1.2827	69

TABLE 5

Hydroxyl Derivatives of Cyclotetrasiloxanes

| Hydroxyclotetrasiloxane | Temperature | | n_D^{20} | $d_.^{20}$ |
	B.p. (press. in mm)	M p		
Pentamethylhydroxycyclotetrasiloxane	100° (20)	−21°	1.4082	1.0478
Hexamethyl-1,5-dihydroxycyclotetrasiloxane	120 (20) sublim.	120	—	—
1-Ethyl-1-hydroxyhexamethylcyclotetrasiloxane	—	−36	1.4230	1.0723
1,5-Diethyl-1,5-dihydroxytetramethylcyclotetrasiloxane		−5	1.4405	1.1711

The tetramer with one $(C_2H_5)HSiO$ unit was obtained in 9.8% yield, while the yield of tetramer with two such units was 10.2%.

Hydrolysis of the mono- and dichlorinated cyclotetrasiloxanes gave the hydroxyl derivatives (Table 5).

All of these hydroxycyclotetrasiloxanes are soluble in alcohols as well as in gasoline hydrocarbons and benzene.

Conditions for the hydrolysis of the chloro derivatives of these tetramers were explored. It was found that only hydroxyl derivatives are obtained in water-ether medium; however, in strongly acid medium, further con-

densation through the hydroxyl groups occurs. The chlorinated derivatives themselves can undergo cohydrolysis. For sample, cohydrolysis of pentamethylchlorocyclotetrasiloxane with an excess of trimethylchlorosilane gave pentamethyltrimethylsiloxycyclotetrasiloxane (A) with a b. p. of 115-116° at 21 mm, m. p. −56°, d_4^{20} 0.9843, $n^{20}D$ 1.4020.

(A)
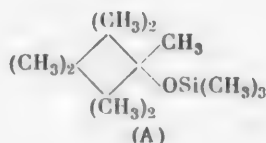
Condensation of pentamethylchlorocyclotetrasiloxane through the hydroxyl groups in acid medium gave bis(heptamethylcyclotetrasiloxanyl)oxide (B), with an m. p. of −36°, d_4^{20} 1.0325, $n^{20}D$ 1.4078.

(B)
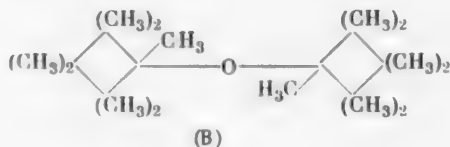
EXPERIMENTAL

129 g of dimethyldichlorosilane (55.10% Cl, 54.98% calculated), 57 g of methyldichlorosilane (61.30% Cl, 61.66% calculated), 370 g of ice, and 370 ml of ether were used in the cohydrolysis of methylchlorosilanes. The ether was added in two equal portions to the methylchlorosilanes, and the mixture was introduced into the hydrolysis apparatus which already contained the ice. Hydrolysis was continued for 1 hour. A temperature of −4 to 4° was maintained during the hydrolysis by cooling the reaction flask. A total of 1860 g of methylchlorosilanes was hydrolyzed, from which was obtained 1065 g of hydrolysis products. 435 g of volatiles was obtained by distillation at 20-70° and 1 mm, and these products were fractionated in a column of 18 theoretical plates. The kettle product from the hydrolysis products (628 g) was cracked at 300-360° in a stream of nitrogen. The nitrogen was freed from oxygen by passage through a tube containing freshly reduced copper at 400°. The 585 g of liquid products obtained from the thermal cracking was fractionated.

7.5, 60, and 100 g, respectively, of penta-, hexa-, and heptamethylcyclotetrasiloxanes were chlorinated, and 9, 62, and 83 g, respectively, were obtained after distillation of the products. Heptamethylchlorocyclotetrasiloxane was separated in a fractionation column. The hexa- and pentamethylchlorocyclotetrasiloxanes were separated by distillation from a Wurtz flask. The analytical results are presented in Table 6.

Methylethylcyclosiloxanes were prepared similarly by cohydrolysis of 330 g of $C_2H_5SiHCl_2$ and 1000 g of $(CH_3)_2SiCl_2$. From 480 g of thermally cracked product were obtained:

1,1,3,3,5,5-Hexamethyl-7-ethylcyclotetrasiloxane (47 g).

Found %: H(−Si) 0.36; C 32.36; H 8.14. M 295; MR 74.97. $C_8H_{24}O_4Si_4$. Calculated %: H(−Si) 0.34; C 32.42; H 8.11. M 296; MR 74.82.

1,1,5,5-Tetramethyl-3,7-diethylcyclotetrasiloxane (49 g).

Found %: H(−Si) 0.65; C 32.65; H 8.02. M 289; MR 75.33. $C_8H_{24}O_4Si_4$. Calculated %: H(−Si) 0.67; C 32.42; H 8.11. M 296; MR 75.08.

Chlorination of these compounds gave:

1-Ethyl-1-chlorohexamethylcyclotetrasiloxane.

Found %: Cl 11.30. $C_8H_{23}O_4ClSi_4$. Calculated %: Cl 11.21.

1,5-Diethyl-1,5-dichlorotetramethylcyclotetrasiloxane.

Found %: Cl 20.40. $C_8H_{22}O_4Cl_2Si_4$. Calculated %: Cl 19.45.

The chlorides were diluted with a 4-fold amount of ether and hydrolyzed at temperatures of −2 to +2° to obtain the hydroxyl derivatives.

Pentamethylhydroxycyclotetrasiloxane.

Found %: OH 5.65, 5.87. MR 70.19. $C_7H_{22}O_5Si_4$. Calculated %: OH 5.70. MR 70.47.

TABLE 6

Results of Analyses of the Alkylcyclosiloxanes

Cyclosiloxane	% C		% H		% H (−Si)		% Si		M		MR	
	Found	Calculated	Found	Calculated	Found	Calculated	Found	Calculated	Found	Calculated	Found	Calculated
Pentamethylcyclotetra-siloxane	23.89	23.59	7.15	7.12	1.10	1.10	43.95	44.11	260	254	62.13	61.45
Hexamethylcyclotetra-siloxane	26.83	26.83	7.53	7.51	0.75	0.75	41.77	41.81	264	268	66.18	65.82
Heptamethylcyclotetra-siloxane	30.06	29.81	7.78	7.86	0.40	0.36	39.68	39.80	276	282	70.78	70.19
Heptamethylchloro-cyclotetrasiloxane	26.88	26.54	6.43	6.63	11.26	11.22	35.30	35.40	316	316.5	—	—
Hexamethyldichloro-cyclotetrasiloxane	21.13	21.36	5.26	5.37	21.00	21.01	33.35	33.26	332	337	—	—
Pentamethyltrichloro-cyclotetrasiloxane	16.39	16.78	4.50	4.22	29.84	29.74	—	—	363	358	—	—

Hexamethyl-1,5-dihydroxycyclotetrasiloxane.

Found %: OH 11.20, 11.38. $C_6H_{20}O_6Si_4$. Calculated %: OH 11.32.

1-Ethyl-1-hydroxyhexamethylcyclotetrasiloxane.

Found %: OH 5.64. MR 75.20. $C_8H_{24}O_5Si_4$. Calculated %: OH 5.75. MR 75.10.

1,5-Diethyl-1,5-dihydroxytetramethylcyclotetrasiloxane.

Found %: OH 9.80, 9.84. MR 73.88. $C_8H_{24}O_6Si_4$. Calculated %: OH 10.36. MR 75.64.

Heptamethyltrimethylsiloxycyclotetrasiloxane was prepared by cohydrolysis of 31.6 g of heptamethyl-chlorocyclotetrasiloxane with 108.6 g of trimethylchlorosilane. Fractionation gave 13 g of a substance which, in spite of a second distillation, showed a deviation in the MR value.

Found %: Si 37.60; C 31.95; H 8.01. M 359; MR 91.67. $C_{10}H_{30}O_5Si_5$. Calculated %: Si 37.82; C 32.40; H 8.16. M 370.6; MR 93.20.

Bis(heptamethylcyclotetrasiloxanyl)oxide was prepared in a yield of 85.4%.

Found %: C 29.57; H 7.32. MR 138.04. $C_{14}H_{42}O_9Si_8$. Calculated %: C 29.06; H 7.26. MR 137.48.

SUMMARY

1. 14 alkylcyclotetrasiloxanes, containing H, Cl, and OH on the silicon atoms, were obtained from the products of the cohydrolysis of dimethyldichlorosilane with methyl- and ethyldichlorosilane.

2. Heptamethyltrimethylsiloxycyclotetrasiloxane and bis(heptamethylcyclotetrasiloxanyl)oxide were synthesized.

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•Original Russian pagination. See C. B. translation.

INVESTIGATIONS IN THE FIELD OF ORGANOCYCLOSILOXANES

VI. RING FORMATION DURING COHYDROLYSIS OF ALKYLDI- AND TRICHLOROSILANES

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The extremely important, in a practical sense, cohydrolysis of monomers with functionalities of 2 and 3 has received almost no study at all from the point of view of theory. The difficulties involved in such a study are quite understandable, since products of three-dimensional condensation are obtained. In view of the great tendency of organosilicon compounds toward cyclization during hydrolysis, the formation of linear structures with cyclic units during cohydrolysis, of monomers with functionalities of 2 and 3 undoubtedly occurs.

Both during hydrolysis of trifunctional monomers alone, and during cohydrolysis, of monomers with functionalities of 2 and 3, the amount of residual hydroxyl groups is found to lie within the limits of 1 to 2%. Moreover, the hydrolysis products remain soluble and fusible. This circumstance can be explained only on the basis that the trifunctional component enters into the ring structures; otherwise, three-dimensional infusible and insoluble polymers would be formed.

It was previously proposed [1] that the mechanism of the action of the majority of catalysts on the curing of such polymers is based on reactions in which the rings present in the hydrolysis products are polymerized. A study of the increase in the viscosity in the presence of NaOH of resins prepared from dimethyldichloro- and phenyltrichlorosilanes showed that the hydrolysis products contain a three-ring linear structure [2].

Fromberg came to this same conclusion [3] on the basis of determinations of the rate of gel formation of resins prepared from methyltrichloro-, dimethyldichloro-, and phenyltrichlorosilanes. The authors of the papers cited above consider that, under the action of the catalysts, polymerization of the rings occurs with subsequent formation of macrorings or cross-linked chains.

In studying the structure of polymers with functionalities of 2 and 3, we undertook the cohydrolysis of the previously synthesized [4] hexamethyl-1,5-dichlorocyclotetrasiloxane with dimethyldichlorosilane in order to obtain ring-containing linear structures and to compare them with the products of the cohydrolysis of methyltrichlorosilane and dimethyldichlorosilane. The cohydrolyses were carried out at the different mole ratios indicated in Table 1. The hydrolysis products were polymerized with 4% of a 50% aqueous solution of KOH at 21°; the reaction mixture was stirred during the polymerization. The experiments were continued to gel formation. The instant of gel formation can be sharply fixed within the limits of 5-10 seconds.

In order to obtain specific ring-containing linear structures, parallel reactions were carried out in which $(CH_3)_2SiCl_2$ was cohydrolyzed with hexamethyl-1,5-dichlorocyclotetrasiloxane, and the hydrolysis products were polymerized under the same conditions. It was not possible to obtain hydrolysis products in which the ratio $CH_3SiCl_3:(CH_3)_2SiCl_2$ was greater than 1:0.667, since the hydrolysis products were partially gelled even when two volumes of toluene were introduced into the reaction medium.

In calculating the ratios of $RSi{\lessapprox}$ to $R_2Si{<}$, use was made of the fact that the product of the hydrolysis of hexamethyl-1,5-dichlorocyclotetrasiloxane can be considered as the product of the cohydrolysis of 2 molecules of R_2SiCl_2 and 2 molecules of $RSiCl_3$:

$$2Cl-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{Si}}-Cl + 2Cl-\underset{\underset{Cl}{|}}{\overset{\overset{CH_3}{|}}{Si}}-Cl \xrightarrow{H_2O}$$
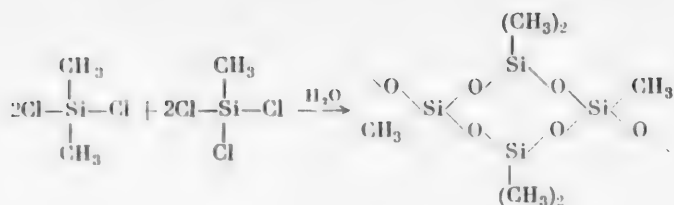
In either case, two R_2Si units and two silsesquioxane units, $RSi-O_{0.5}$ with $O_{0.5}$ above and $O_{0.5}$ below, are obtained.

At a ratio of, for example, 1 mole of dimethyldichlorosilane to 1 mole of hexamethyl-1,5-dichlorocyclotetrasiloxane we obtained the following linear polymer (a square denotes an $(Si-O)_4$ ring:
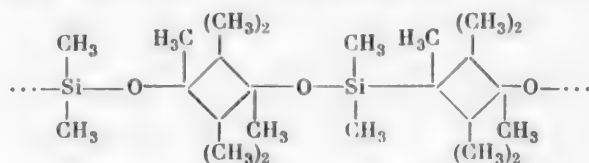
The same polymer with a ratio of $RSi\lesseqgtr$ to $R_2Si\lessdot$ of 0.667 is obtained (theoretically) during hydrolysis of 1.5 moles of dimethyldichlorosilane with 1 mole of methyltrichlorosilane.

The poly(hexamethylcyclotetra)siloxane obtained by hydrolysis of hexamethyl-1,5-dichlorocyclotetrasiloxane has a ratio of $RSi\lesseqgtr$ to $R_2Si\lessdot$ of 1.
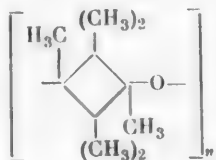
Considering the cohydrolysis data (Table 1), it can be seen that the product of the hydrolysis of dimethyldichlorosilane alone had not formed a gel after more than two days. The product of the cohydrolysis of 1 mole of hexamethyl-1,5-dichlorocyclotetrasiloxane with 50 moles of dimethyldichlorosilane polymerized in 245 minutes. The gel-formation time decreased sharply when the component ratio was 1:10, and it reached a minimum (4 minutes) at a ratio of 1:1. Poly(hexamethylcyclotetra)siloxane formed a gel in twice the time, 8 minutes, probably owing to steric hindrance.

Analysis of the products of the hydrolysis of dimethyldichlorosilane with methyltrichlorosilane and with hexamethyl-1,5-dichlorocyclotetrasiloxane at a ratio of $RSi\lesseqgtr$ to $R_2Si\lessdot$ of 0.286 showed that the OH-group content was, respectively, 1.57 and 1.08%. However, treatment of these two hydrolysis products with 4% of concentrated hydrochloric acid not only did not lead to gel formation, but did not even increase the viscosity during a treatment time 10 times longer than in the case when KOH was used. This experiment conclusively showed that the cause of gel formation is rupture of the rings during polymerization; HCl is a good condensation catalyst for hydroxysilanes, but is not a catalyst for the polymerization of rings.

A rapid decrease in the gel-formation time with an increase in the portion of CH_3SiCl_3 was found for products of the hydrolysis of $(CH_3)_2SiCl_2$ and CH_3SiCl_3. The figure clearly shows that, in this case, gel formation

proceeds with the same regularity, but sets in more slowly than in the case of the products of the hydrolysis with hexamethyl-1,5-dichlorocyclotetrasiloxane.

In general, rings with silsesquioxane units readily undergo polymerization. This can be shown using the three cyclic compounds as an example (Table 2).
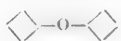
TABLE 1

Polymerization of Cohydrolysis Products with a Functionality of 2 and 3

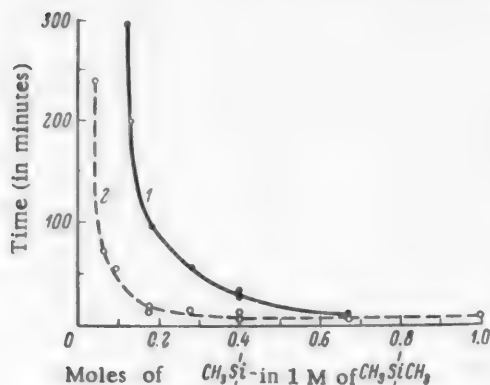| Monomers (in moles)			Moles $RSi \lessgtr$ to $R_2Si \lessgtr$	n_D^{20}	Time of gel formation from start of reaction (minutes)
Dimethyl-chloro-silane	Methyl-trichloro-silane	Hexa-methyl-1 5-dichlo-rocyclo-tetrasil-oxane			
1.5	1	0	0.667	1.4150	4.3
2.5	1	0	0.400	1.4109	24
3.5	1	0	0.286	1.4088	54
5.5	1	0	0.182	1.4075	95
7.5	1	0	0.133	1.4070	201
8	1	0	0.125	1.4068	298
1	0	0	0.0	1.4022	48 hours
0	0	1	1.0	1.4160	8
1	0	1	0.667	1.4158	4
3	0	1	0.400	1.4117	6.5
5	0	1	0.286	1.4100	14
10	0	1	0.167	1.4079	18
20	0	1	0.091	1.4050	56
30	0	1	0.062	1.4041	72
50	0	1	0.038	1.4039	245

TABLE 2

The Effect of Silsesquioxane Units on Polymerization Rate

Cyclic tetramer	Conventional formula	d_4^{20}	n_D^{20}	Melting point	Time of polymeriza-tion to gel
Octamethylcyclo-tetrasiloxane	◇	0.9558	1.3968	17.4°	>60 days
Bis(heptamethylcyclo-tetrasiloxane	◇—o—◇	1.0352	1.4078	—36	62 hours
Poly(hexamethyl-cyclotetra)siloxane	$[...◇—o...]_n$	1.1277	1.4160	~0	8 minutes

The lag in rate of gel formation of polymers based on CH_3SiCl_3 is completely clear. In this case, all three trifunctional groups do not participate in the formation of rings; part of these groups form branched or cross-linked structures. In this connection, the number of dimethyldichlorosilane molecules entering into the composition of the linear portion of the polymer and of the dimethylcyclosiloxane rings is increased. But neither branched nor closed cyclic compounds are polymerized by the action of 4% of KOH at 21°.

The refractive indices of both types of hydrolysis products are very characteristic. When methyltrichlorosilane is one of the components, the index of refraction is somewhat lower, but the values of $n^{20}D$ are comparable, showing that the structures of these two types of compounds are similar.

The refractive index of octamethylcyclotetrasiloxane, which is the most easily formed during hydrolysis, is 1.3968, that of linear dimethylpolysiloxanes is 1.4044, and that of the product of the hydrolysis of dimethyl-dichlorosilane is 1.4022. The increase in $n^{20}D$ to 1.4150-1.4160 in cohydrolyzed polymers is a consequence of the large number of silsesquioxane units.

Analyzing all of these data, we are led to the conclusion that cyclic structures with silsesquioxane units are formed during the process of cohydrolysis of dimethyldi- and methyltri-chlorosilanes. With a high content of the trifunctional component, these rings are probably tetramers of the type

Time vs gel formation of hydrolysis products of dimethyldichlorosilane with methyltrichloro-silane (1) and with hexamethyl-1,5-cyclotetra-siloxane (2).
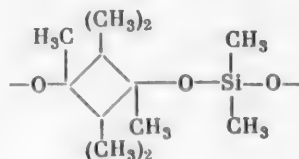

or possibly are partially trimers, pentamers, and hexamers. The higher rings should rupture with difficulty.

With a lower content of the trifunctional component, the formation of blocking rings is possible.
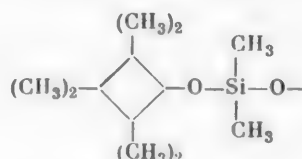
With a decrease in the functionality of the hydrolyzing system, macrorings and, in even greater amount, branched structures and closed cyclic compounds of the type $(R_2SiO)_h$ are formed owing to hydrolysis of one di-functional component. There is also the possibility of the formation of individual condensed cyclic compounds of the type isolated by Scott [5], for example, with subsequent polymerization of these compounds.

The occurrence of polymerization of rings to linear systems containing rings is also confirmed by the case in which the silicon atom carries an ethyl radical. Cohydrolysis of 5 moles of dimethyldichlorosilane with 1 mole of 1,5-diethyl-1,5-dichlorotetramethylcyclotetrasiloxane [4] gave a polymer with the structural unit
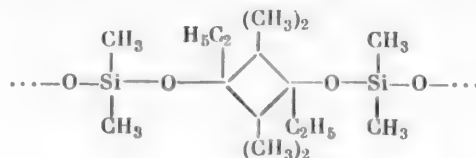
This polymer formed a gel in 11 minutes.

EXPERIMENTAL

The cohydrolysis was carried out with three parts of water and two parts of toluene at 20-25°. The toluene was distilled in a fractionation column. A control analysis was carried out on the products of the hydrolysis of CH_3SiCl_3 with $(CH_3)_2SiCl_2$ at a mole ratio of 0.400.

Found %: C 28.21; H 7.14. $C_{12}H_{36}O_8Si_7$. Calculated %: C 28.57; H 7.14.

In the case of the hydrolysis of hexamethyl-1,5-dichlorocyclotetrasiloxane and $(CH_3)_2SiCl_2$ at this same ratio, 0.400, analysis gave, in %: H, 6.99; C, 28.33.

The polymerization experiments were carried out with 5 g of hydrolysis products; stirring was at the rate of 315 revolutions per minute. Experiments lasting more than a day were carried out with KOH dissolved in isobutyl alcohol. A control experiment with the product of the hydrolysis of 0.400 mole of methyltrichlorosilane gave a gel time of 27 minutes instead of 24 minutes; i. e., the time was increased by 11.25% when isobutyl alcohol was used.

SUMMARY

1. Complex ring-containing linear structures with silsesquioxane*units are formed during cohydrolysis of alkylchlorosilanes with functionalities of 2 and 3.

2. Silsesquioxane units in alkylcyclosiloxanes polymerize more rapidly than siloxane units.

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INVESTIGATIONS IN THE FIELD OF ORGANOCYCLOSILOXANES

VII. CYCLIZATION DURING THE HYDROLYSIS OF ALKYLCHLOROSILOXANES

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Alkylsiloxanes with functional groups, in particular, those with mixed members, can be synthesized by the method of heterofunctional polycondensation [1].

Alkylsiloxanes with functional groups can be used for the synthesis of new compounds. In addition, the hydrolysis of alkylsiloxanes, either completely or to the stage in which hydroxysilanes are obtained, is of interest for the investigation of the mechanism of the hydrolysis as a whole and, in particular, for determining the degree of cyclization during hydrolysis.

Alkyl-α, ω-dichlorosiloxanes can be used for obtaining the corresponding dihydroxysiloxanes. The hydrolysis is best carried out with cooling to -5° in diethyl ether, chlorosilane being poured rapidly into a solution of caustic soda [2].

Hydroxy derivatives of the series $HO(-Si(CH_3)_2O-)_{2-5}H$] were obtained from alkyl-α,ω-dichlorosilanes by hydrolysis under the above-mentioned conditions; the properties of these derivatives are given in Table 1.

TABLE 1

Alkyldihydroxysiloxanes $HO[-Si(CH_3)_2O-]_{2-5}H$

Alkyldihydroxysiloxanes	Formula	Melting point	d_4^{20}	n_D^{20}	Yield (%)
Tetramethyl-1,3-di-hydroxydisiloxane	$HO\left[-\overset{CH_3}{\underset{CH_3}{Si}O}-\right]_2 H$	67°	—	—	88
Hexamethyl-1,5-di-hydroxytrisiloxane	$HO\left[-\overset{CH_3}{\underset{CH_3}{Si}O}-\right]_3 H$	—23	0.9950	1.4090	74
Octamethyl-1,7-dihydro-xytetrasiloxane	$HO\left[-\overset{CH_3}{\underset{CH_3}{Si}O}-\right]_4 H$	—5	0.9881	1.4088	76
Decamethyl-1,9-di-hydroxypentasiloxane	$HO\left[-\overset{CH_3}{\underset{CH_3}{Si}O}-\right]_5 H$	—43	0.9807	1.4086	55

Tetramethyl-1,3-dihydroxydisiloxane was obtained previously by other methods [3, 4]. The solubility of tetramethyl-1,3-dihydroxysiloxane in water was found to be 11.5 g per 100 g of water at 20°, 283 g in ethyl al-

cohol, 161 g in dioxane and 156 g in ethylene glycol. Hexamethyl-1,5-dihydroxytrisiloxane and the higher hydroxysiloxanes of this series are insoluble in water but dissolve in gasoline, benzene and toluene.

Like the hydrolysis of dimethyldichlorosilane, the hydrolysis of dimethyl-α,ω-dichlorosiloxanes in an acid medium gives (Table 2) approximately 50% linear and 50% cyclic compounds (volatile at 200°). Hexamethyl-1,5-dichlorotrisiloxane, which gave only 12% cyclic compounds, was an exception.

The hydrolysis of the same compounds dissolved in three parts of ether results in almost complete cyclization (Table 2). In other words, 50-63% of the initial difunctional molecules with 3, 4 or 5 silicon atoms undergo intramolecular condensation with the formation of cyclic compounds, while the remaining amount forms higher cyclic compounds during this process.

TABLE 2

Composition of the Hydrolysis Products of Dimethyl-α,ω-Dichlorosiloxanes

Compound hydrolyzed	Number of cyclic comps. as a result of hydrolysis (%)		
	In water	In ethereal solution	
		Total	Composition
Tetramethyl-1,3-dichlorodisiloxane	50	95	Tetramer 57, Hexamer 6.5, Octamer 11
Hexamethyl-1,5-dichlorotrisiloxane	12	96	Trimer 62, Hexamer 30
Octamethyl-1,7-dichlorotetrasiloxane	64	96	Tetramer 63, octamer 35
Decamethyl-1,9-dichloropentasiloxane	50	89	Pentamer ~50, Decamer ~35

The hydroxy derivatives can be obtained comparatively easily by the hydrolysis of other alkylchlorosiloxanes. For example, the hydrolysis of octamethyl-3,5-dichlorotetrasiloxane gives a 75% yield of octamethyl-3,5-dihydroxytetrasiloxane, with an m. p. of -27°, $n^{20}D$ 1.4074, d_4^{20} 0.9982.

$$\underset{\underset{OH}{|}}{(CH_3)_3Si-O-\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{Si}}-O-\overset{\overset{CH_3}{|}}{Si}-O-Si(CH_3)_3}$$
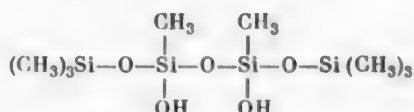
The hydrolysis of alkyl-α,ω-dichlorosiloxanes in an acid medium gives a possibility of obtaining cyclic compounds with identical or mixed members. The hydrolysis is carried out with two parts of water and two parts of ethyl ether. The alkylcyclosiloxanes obtained are given in Table 3.

An examination of the data of Table 3 shows that cyclic tetramers may be obtained from the hydrolysis products of dichlorodisiloxanes, while cyclic hexamers may be obtained from the hydrolysis of dichlorotrisiloxanes. Exceptions are: 1,1,3-trimethyldichlorodisiloxane, which gave a trimer (III) and a hexamer (IV) as a result of hydrolysis, and 1,1,3,3-tetramethyl-5,5-diethyldichlorotrisiloxane which gave a trimer (IX) when hydrolyzed. We did not succeed in isolating the higher cyclic compounds but they were found to be present in an amount of 8-30% in all cases by a volatility test (at 200° in a box).

The presence of ethyl radicals favors cyclization to a greater extent than the presence of methyl radicals or hydrogen near the silicon atom; this is evident from the yields obtained by hydrolysis.

The characteristics of the alkylcyclosiloxanes obtained, of which (III) -(IX) were prepared for the first time, are given in Table 4.

As regards their properties, the cyclic compounds obtained agree with already-known cyclic compounds containing the same members at the silicon atom.

TABLE 3

Alkylcyclosiloxanes Obtained by the Hydrolysis of Alkylchlorosiloxanes

Compounds hydrolyzed	Alkylcyclosiloxanes obtained	Formula	Yield (%)
(structure) (I)	Tetramethylcyclo-tetrasiloxane	$\left[\begin{array}{c} CH_3 \\ -Si-O \\ H \end{array}\right]_4$	32.0
(structure) (II)	Hexamethylcyclo-hexasiloxane	$\left[\begin{array}{c} CH_3 \\ -Si-O \\ H \end{array}\right]_6$	11.4
(structure) (III)	1,1,3,5,5,7-Hexa-methylcyclotetra-siloxane	$\left[\begin{array}{cc} CH_3 & CH_3 \\ -Si-O-Si-O \\ CH_3 & H \end{array}\right]_2$	21.2
(structure) (IV)	1,4,3,5,5,7,9,9,11-Nonamethylcyclo-hexasiloxane	$\left[\begin{array}{cc} CH_3 & CH_3 \\ -Si-O-Si-O \\ CH_3 & H \end{array}\right]_3$	5.5
(structure) (V)	1,1,3,5,7,7,9,11-Octamethylcyclo-hexasiloxane	$\left[\begin{array}{ccc} CH_3 & CH_3 & CH_3 \\ -Si-O-Si-O-Si-O \\ CH_3 & H & H \end{array}\right]_2$	18.4
(structure) (VI)	1,1,5,5-Tetramethyl-3,3,7,7-tetraethyl-cyclotetrasiloxane	$\left[\begin{array}{cc} C_2H_5 & CH_3 \\ -Si-O-Si-O \\ C_2H_5 & CH_3 \end{array}\right]_2$	39.5
(structure) (VII)	1,1,5,5-Tetramethyl-3,7-diethylcyclo-tetrasiloxane	$\left[\begin{array}{cc} C_2H_5 & CH_3 \\ -Si-O-Si-O \\ H & CH_3 \end{array}\right]_2$	48.4
(structure) (VIII)	1,1,7,7-Tetramethyl-3,5,9,11-tetraethyl-cyclohexasiloxane	$\left[\begin{array}{ccc} CH_3 & C_2H_5 & C_2H_5 \\ -Si-O-Si-O-Si-O \\ CH_3 & H & H \end{array}\right]_2$	10.4
(structure) (IX)	1,1,3,3-Tetramethyl-diethylcyclotri-siloxane	$\begin{array}{ccc} CH_3 & CH_3 & C_2H_5 \\ Si-O-Si-O-Si-O \\ CH_3 & CH_3 & C_2H_5 \end{array}$	41.8

TABLE 4

Characteristics of Alkylcyclosiloxanes

Alkyl-cyclosil-oxanes	Boiling point (pressure in mm)	Melting point	n_D^{20}	d_4^{20}	MR	
					Found	Calculated
(I)	134° (750)	—	1.3872	—	—	—
(II)	47 (2)	—	1.3942	—	—	—
(III)	57 (18)	—40°	1.3930	0.9680	65.88	65.82
(IV)	69 (0.5)	—78	1.3980	0.9754	99.44	98.73
(V)	70—72 (6)	—95	1.3965	0.9961	93.72	94.36
(VI)	75 (0.5)	—68	1.4155	0.9573	92.17	93.08
(VII)	68—70 (6)	—88	1.4055	0.9596	75.68	75.08
(VIII)	72—73 (6)	—52	1.4115	0.9821	112.36	112.88
(IX)	56 (6)	—8	1.4071	0.9583	64.23	65.18

At 20° all the compounds obtained are transparent liquids, polymerized with varying degrees of rapidity by sulfuric acid with rupture of the rings.

An attempt was made to synthesize tetramethyl-1,3-diaminodisiloxane by the ammonolysis of tetramethyl-1,3-dichlorodisiloxane.

However, in spite of the mild conditions of the experiment (reaction temperature -71°, liquid ammonia, dilution with ether) a 65.5% yield of bis (tetramethyldisilanamine)-cyclodioxide (X) was obtained instead of the expected substance.
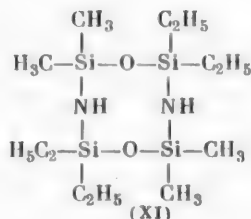
$$
\begin{array}{cc}
CH_3 & CH_3 \\
| & | \\
H_3C-Si-O-Si-CH_3 \\
| & | \\
NH & NH \\
| & | \\
H_3C-Si-O-Si-CH_3 \\
| & | \\
CH_3 & CH_3 \\
& (X)
\end{array}
$$
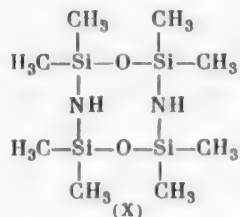
This heterocyclic compound has a new interesting feature: the siloxane bonds alternate with silamine bonds. The cyclodioxide has an m. p. of 40° and a b. p. of 106-107° at 23 mm; it crystallizes as prisms or needles. It is soluble in ether, gasoline, benzene, acetone, alcohol, dichloroethane, chlorobenzene, carbon tetrachloride and ethyl Cellosolve. It may be kept in a sealed flask without decomposition for more than a year. It is insoluble and stable in water and a 2.5 N solution of NaOH. It is slowly decomposed by 1 N acetic acid and rapidly decomposed by 1 N hydrochloric acid. The result of the reaction with HCl is the formation of dimethylpolysiloxanes, with $n^{20}D$ 1.4040. The high degree of the latter is evidently caused by the blocking action of the amino groups during hydrolysis in a solution of HCl.

Similarly, a yield of 44% of bis(dimethyldiethyldisilanamine)-cyclodioxide (XI) was obtained from 1,1-dimethyl-3,3-diethyldichlorodisiloxane;

$$
\begin{array}{cc}
CH_3 & C_2H_5 \\
| & | \\
H_3C-Si-O-Si-C_2H_5 \\
| & | \\
NH & NH \\
| & | \\
H_5C_2-Si-O-Si-CH_3 \\
| & | \\
C_2H_5 & CH_3 \\
& (XI)
\end{array}
$$

the b. p. was 70° at 0.5 mm, the m. p. was < 20°, $n^{20}D$ 1.4308. Its properties are roughly the same as those of the previous ring.

EXPERIMENTAL

The preparation of dimethyldihydroxysiloxanes was carried out by the hydrolysis of 15 g of the corresponding dimethyldichlorosiloxanes in ether (10-fold amount). The theoretical amount of caustic soda was used for neutralizing the hydrolyzate. The neutral hydrolyzate was dried with potash or was filtered 5-6 times through filter paper to dry it. The ether was distilled off under vacuum.

Tetramethyl-1,3-dihydroxydisiloxane.

Found %: OH 20.40, 20.51. $C_4H_{12}OSi(OH)_2$. Calculated %: OH 20.50.

Hexamethyl-1,5-dihydroxytrisiloxane.

Found %: OH 15.35, 14.86. MR 59.60. $C_6H_{18}O_2Si_3(OH)_2$. Calculated %: OH 15.00. MR 59.80.

Octamethyl-1,7-dihydroxytetrasiloxane.

Found %: OH 9.53, 9.87. MR 78.30. $C_8H_{24}O_3Si_4(OH)_2$. Calculated %: OH 10.82. MR 78.58.

5 g of tetramethylcyclotetrasiloxane (I) ($n^{20}D$ 1.3872, according to data [5] 1.3870) was obtained by the hydrolysis of 22 g of 1,3-dimethyl- 1,3-dichlorotrisiloxane.

Found %: H (−Si) 1.61. $C_4H_{12}O_4(SiH)_4$. Calculated %: H(−Si) 1.68.

5 g of hexamethylcyclohexasiloxane (II) ($n^{20}D$ 1.3942, according to data [5] 1.3870) was obtained by the hydrolysis of 45 g of 1,3,5-trimethyl- 1,5-dichlorotrisiloxane.

Found %: H(−Si) 1.62. $C_6H_{18}O_6(SiH)_6$. Calculated %: H(−Si) 1.68.

Hexamethylcyclohexasiloxane (III) was obtained by the hydrolysis of 100 g of 1,1,3-trimethyl-1,3-dichlorodisiloxane; the amount formed was 15 g.

Found %: H(−Si) 0.77; H 7.85; C 26.39. M 269. $C_6H_{20}O_4Si_4$. Calculated %: H(−Si) 0.75; H 7.31; C 26.83. M 268.

3.9 g of nonamethylcyclohexasiloxane (IV) was isolated from the same hydrolyzate.

Found %: H(−Si) 0.79; Si 41.64. $C_9H_{30}O_6Si_6$. Calculated %: H(−Si) 0.75; Si 41.81. M 402.

Octamethylcyclohexasiloxane (V) (4 g) was obtained by the hydrolysis of 1,1,3,5-tetramethyl-1,5-dichlorotrisiloxane (28 g). The trimer was not isolated.

Found %: H(−Si) 1.10; H 7.10; C 24.67. M 383. $C_8H_{28}O_6Si_6$. Calculated %: H(−Si) 1.03; H 7.22; C 24.74. M 388.

1,1,5,5-Tetramethyl-3,3,7,7-tetraethylcyclotetrasiloxane (VI) (6 g) was obtained by the hydrolysis of 20 g of 1,1-dimethyl-3,3-diethyldichlorodisiloxane.

Found %: H 8.99; C 40.42; Si 31.69. M 350. $C_{12}H_{32}O_4Si_4$. Calculated %: H 9.07; C 40.90; Si 31.81. M 352.

1,1,5,5-Tetramethyl-3,7-diethylcyclotetrasiloxane (VII) (14 g) was obtained by the hydrolysis of 35 g of 1,1-dimethyl-3-ethyl-1,3-dichlorodisiloxane.

Found %: H(−Si) 0.70; Si 37.56. M 290. $C_8H_{22}O_4Si_4$. Calculated %: H(−Si) 0.68; Si 37.87. M 296.

1,1,7,7-Tetramethyl-3,5,9,11-tetraethylcyclohexasiloxane (VIII) (2.5 g) was obtained by the hydrolysis of 30 g of 1,1-dimethyl-3,5-diethyl-1,5-dichlorotrisiloxane. The trimer was not isolated.

Found %: H(−Si) 0.85; Si 37.83. M 437. $C_{12}H_{36}O_6Si_6$. Calculated %: H(−Si) 0.90; Si 37.82. M 444.

3,3,5,5-Tetramethyldiethylcyclotrisiloxane (IX) (12 g) was isolated from the hydrolysis products of 1,1-diethyl-3,3,5,5-tetramethyldichlorotrisiloxane (35 g).

Found %: H 8.32; C 38.38. M 255. $C_8H_{22}O_3Si_3$. Calculated %: H 8.30; C 38.40. M 250.

Bis (tetramethyldisilanamine)-cyclodioxide (X). 150 g of liquid ammonia was placed in a flask with a stirrer and the temperature was maintained at -71° by cooling with dry ice and acetone. 80 g of tetramethyldichlorodisiloxane in 160 g of dry ether was added from a funnel. The reaction lasted 50 minutes. The ammonia was removed by heating and the mixture was filtered in a current of dry air under vacuum. 40 g of NH_4Cl was obtained (theoretical 40.6 g). The ether was distilled off and the product was distilled at 106-107° (23 mm). 38 g of crystals (65.5%) was obtained.

Found %: N 10.00; Si 37.96; C 32.65; H 8.90. M 288. $C_8H_{26}O_2Si_4N_2$. Calculated %: N 9.5; Si 38.10; C 32.71; H 8.84. M 294.

Bis (dimethyldiethyldisilanamine)-cyclodioxide (XI) was obtained by a similar method.

Found %: Si 31.83; N 7.84. M 345. $C_{12}H_{34}O_2Si_4N_2$. Calculated %: Si 32.00; N 8.00. M 350.

Decamethyl-1,9-dihydroxypentasiloxane.

Found %: OH 8.14, 8.86. MR 97.60. $C_{10}H_{32}O_6Si_5$. Calculated %: OH 8.75. MR 97.36.

Octamethyl-3,5-dihydroxytetrasiloxane.

Found %: OH 11.12, 10.93. MR 78.31. $C_8H_{26}O_5Si_4$. Calculated %: OH 10.82. MR 78.02.

SUMMARY

1. Three new dimethyl-α,ω-dihydroxysilanes and 8 alkylcyclosiloxanes with mixed $S-O$ units were obtained by the hydrolysis of alkylchlorosiloxanes.

2. Two cyclic tetramers with alternate siloxane and silamine bonds were isolated by the ammonolysis of alkylchlorosiloxanes.

3. It was found that the hydrolysis of alkylchlorosiloxanes is subject to the same mechanisms with respect to cyclization as the hydrolysis of alkylchlorosilanes.

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•Original Russian pagination. See C. B. translation.

THE REACTION OF NITROSYL CHLORIDE WITH UNSATURATED HYDROCARBONS

V. THE REACTION OF 1-BUTENE AND 2-METHYL-3-BUTENE WITH NITROSYL CHLORIDE IN THE PRESENCE OF HYDROGEN CHLORIDE. THE PREPARATION OF THE ACYL CHLORIDES OF α-CHLOROISOVALERO AND α-CHLOROBUTYROHY-DROXAMIC ACIDS

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In one of the previous papers [1] it was shown that when nitrosyl chloride reacts with trimethylethylene in the presence of hydrogen chloride the main reaction product is not a dimer of trimethylethylene nitrosochloride but a monomeric oxime of 2-chloro-2-methyl-3-butanone, i. e. the presence of hydrogen chloride assists the rearrangement of the initially formed monomeric chloronitroso compound into a chlorooxime.
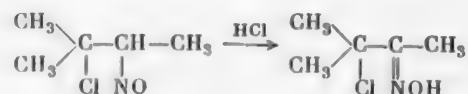
When nitrosyl chloride reacts with 2-methyl-3-butene [2] and butene [3],a solid nitrosochloride is not formed. The main reaction products are the corresponding 1-nitro-2-chloroalkanes and 1,2-dichloroalkanes, i. e. the initially formed monomeric nitrosochloride is oxidized by nitrosyl chloride to the chloronitro compound and the chlorine obtained by the decomposition of the nitrosyl chloride combines with the hydrocarbon to give the dichloride. In consequence, nitrosochlorides of monosubstituted ethylenes do not undergo rearrangement into chlorooximes because their oxidation to the nitro compounds takes place more rapidly.

In order to make a further study of the influence of hydrogen chloride on the rearrangement of a chloro-nitroso compound to the chlorooxime,the reaction of nitrosyl chloride with 2-methyl-3-butene (I) and 1-butene (II) in the presence of hydrogen chloride was also investigated.

The reaction with (I) was carried out in sealed ampoules in a solution of anhydrous ethyl ether with equi-molecular ratios of 2-methyl-3-butene and nitrosyl chloride in the presence of 0.27 mole of hydrogen chloride. The nitrosyl chloride concentration in the ether was the same as in the experiment without hydrogen chloride [2] (4.5 ml of ether per gram of nitrosyl chloride). In the experiments with 1-butene a 50% excess of nitrosyl chloride was taken, its concentration in the ether being reduced(6.25 ml of ether per gram of nitrosyl chloride). To avoid breakage of the ampoules, which occurred in some experiments, in the experiments with 1-butene they were not sealed until a day after the commencement of the reaction.

The particular features of the reaction in the presence of hydrogen chloride should be noted:the reaction velocity is much slower and the pressure developed in the ampoules is far weaker. Whereas in the experiments in which hydrogen chloride was not used [2, 3] the reaction lasted from several hours to one day*, not less than
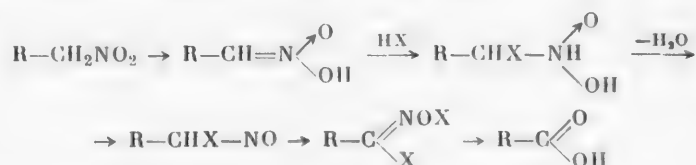
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* The end of the reaction was determined by the change in color of the reaction mixture from red-brown to blue-greenish and greenish-yellow.

two days were required to complete the reaction in the presence of hydrogen chloride. Water, which collected as a small layer on the bottom of the ampule (in the form of a solution of hydrogen chloride) was liberated as a result of the reaction, both in the experiments with 2-methyl-3-butene and 1-butene.

The main reaction products (yield~50%) were the acyl chlorides of α-chloroisovalerohydroxamic and α-chloro-N-butyrohydroxamic acids. In addition, the dichlorides of 3,4-dichloro-2-methylbutane and 1,2-dichloro-butane were obtained, and in the reaction with 2-methyl-3-butene a small amount of 4-nitro-3-chloro-2-methylbutane was formed.

In literature, it is indicated that acyl chlorides of unsubstituted hydroxamic acids can be obtained from aldoximes by the action of chlorine [4] or nitrosyl chloride [5]. In the latter case it was possible to isolate the primary products of the reaction of aliphatic aldoximes with nitrosyl chloride, dimeric gem-chloronitroso compounds, which undergo rearrangement at varying rates into the acyl chlorides of hydroxamic acids. A blue-green or blue color of their solutions is characteristic of gem-nitroso compounds when they occur partly in the monomolecular state. Since colors of this type did not appear during the reaction in our case and gem-chloronitroso compounds were not found in the reaction products, they could hardly be intermediate reaction products here.
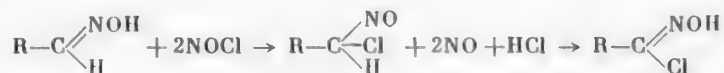
A number of investigators assume [6] that hydroxamic acids and their acyl chlorides form an intermediate stage in the hydrolysis of primary nitro compounds into carboxylic acids under the influence of strong mineral acids. The reaction is presumed to proceed according to the system

$$R-CH_2NO_2 \rightarrow R-CH=N\begin{smallmatrix}O\\\\OH\end{smallmatrix} \xrightarrow{HX} R-CHX-NH\begin{smallmatrix}O\\\\OH\end{smallmatrix} \xrightarrow{-H_2O}$$

$$\rightarrow R-CHX-NO \rightarrow R-C\begin{smallmatrix}NOX\\\\X\end{smallmatrix} \rightarrow R-C\begin{smallmatrix}O\\\\OH\end{smallmatrix}$$

where X = Cl, OSO_3H

In a special experiment it was shown that, being soluble in ether containing hydrogen chloride, 4-nitro-3-chloro-2-methylbutane, which in this case could form the initial product for obtaining the acyl chloride of α-chloroisovalerohydroxamic acid, does not undergo any change on standing for several weeks at room temperature. In consequence, the nitrochloro compound can hardly be an intermediate product in the reaction for the preparation of the acyl chlorides of α-chlorohydroxamic acids.
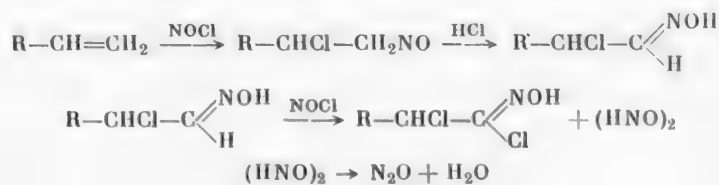
In Rheinboldt's work [5] the course of the reaction is expressed by the general system

$$R-C\begin{smallmatrix}NOH\\\\H\end{smallmatrix} + 2NOCl \rightarrow R-C\begin{smallmatrix}NO\\\\Cl\\\\H\end{smallmatrix} + 2NO + HCl \rightarrow R-C\begin{smallmatrix}NOH\\\\Cl\end{smallmatrix}$$

Since in all our experiments the reaction was always accompanied by the liberation of water, the system of the reaction in the presence of hydrogen chloride must be different.

It may be assumed that the formation of water takes place as a result of the decomposition of hyponitrous acid [14]. The latter can be obtained by the action of nitrosyl chloride on the oxime.

What has been said above makes it possible to assume the following possible reaction for the formation of the acyl chlorides of α-chlorohydroxamic acids.

$$R-CH=CH_2 \xrightarrow{NOCl} R-CHCl-CH_2NO \xrightarrow{HCl} R-CHCl-C\begin{smallmatrix}NOH\\\\H\end{smallmatrix}$$

$$R-CHCl-C\begin{smallmatrix}NOH\\\\H\end{smallmatrix} \xrightarrow{NOCl} R-CHCl-C\begin{smallmatrix}NOH\\\\Cl\end{smallmatrix} + (HNO)_2$$

$$(HNO)_2 \rightarrow N_2O + H_2O$$

where R = C_2H_5, iso-C_3H_7

The chloronitro compound obtained in the first stage of the reaction is converted to the chlorooxime under the influence of hydrogen chloride. With nitrosyl chloride the chlorooxime gives the acyl chloride of α-chloro-substituted hydroxamic acid and hyponitrous acid, which decomposes into nitrous oxide and water.

The possibility that water is also formed by the oxidation of hydrogen chloride by nitric oxides (for example, N_2O_3) [14] is not excluded.

EXPERIMENTAL

Initial products. 2-Methyl-3-butene was obtained by the dehydration of isoamyl alcohol over anhydrous aluminum sulfate at 380-420°. The hydrocarbon condensate was distilled over metallic sodium in a column with 20 theoretical plates. The fraction with a b. p. of 20.5-21.5° at 767 mm, $n^{15}D$ 1.3683 was separated.

1-Butene was synthesized from allyl bromide and magnesium methyl iodide [7] and was used for the reaction without further purification.

Nitrosyl chloride was obtained by the reaction of a concentrated solution of sodium nitrite with hydrochloric acid (d 1.19) [8]. The product was heated to boiling for 30-40 minutes with a reflux condenser (minus 40-50°) and was then distilled.

The reaction of nitrosyl chloride with 2-methyl-3-butene in the presence of hydrogen chloride. 71 g of cooled 2-methyl-3-butene was added to 10 g of hydrogen chloride in 300 ml of anhydrous ether, cooled to -12°, and 66 g of nitrosyl chloride, cooled to -50°, was then added with stirring. The brown-red solution was poured into 11 ampoules, cooled with ice and salt. The ampoules were sealed and placed in a water bath +7°). The next day (bath temperature + 14°) the reaction mixture had a brown color which showed no tinge of red, and a small layer of a colorless transparent liquid* had collected on the bottom of the ampoules. After a day the color of the ethereal solution was again greenish-yellow. The ampoules were cooled to -50° and were sealed by heating the end in the flame of a burner, a weaker pressure being noted than in the experiments where hydrogen chloride was not used [2, 3]. The contents of the ampoules were washed with three quantities of water (total volume 400 ml); 4.97 g of hydrogen chloride was found in the wash water. The following were distilled from the initial reaction products in a column with 20 theoretical plates: the initial hydrocarbon (b. p. 20-28°, main volume below 25°, weight 24 g), ether and 3,4-dichloro-2-methylbutane with a b. p. of 142-147° at 766 mm, weight 12.5 g (according to data [9]: b. p. 143-145°).

When the residue was distilled from a Favorsky flask a fraction with a b. p. of 65-75° at 3 mm, weight 46.5 g, was obtained. The residue was 10.5 g. After several distillations of the main fraction the following fractions were obtained: 1st, b. p. 58-61° at 2 mm, 3.1 g $n^{20}D$ 1.4588 (4-nitro-3-chloro-2-methylbutane; according to data [2]: b. p. 76-77° at 7 mm, $n^{20}D$ 1.4548); 2nd, b. p. 65-66° at 1 mm, 17.8 g; 3rd, b. p. 66-67° at 1 mm, 10.6 g, $n^{20}D$ 1.4868. The two latter fractions represented the acyl chloride of α-chloroisovalerohydroxamic acid.

For the 65-66° at 1 mm fraction: d_4^{20} 1.2375, $n^{20}D$ 1.4877, MR_D 39.57; calc. 39.35.

Found %: Cl 41.23, 41.23 (Carius). $C_5H_9ONCl_2$. Calculated %: Cl 41.70.

The substance was soluble in ether, alcohol, benzene and gasoline (b. p. 60-80°). It was insoluble in water in the cold, with heating it decomposed; the solution contained chlorine ions. An aqueous solution gave a qualitative reaction for hydroxamic acid with ferric chloride. With increasing hydrolysis of the acyl chloride, as a result of heating the pale-red color of the solution changed to dark red.

When kept in a closed vessel the substance gradually decomposed and colorless crystals were formed, the amount of which increased with time. The crystals were insoluble in ether but readily soluble in water. The aqueous solution gave a precipitate with a solution of silver nitrate, it reduced Fehling solution in the cold and gave a reaction for hydroxylamine [10]. When the crystals were acted on by a solution of alkali a strong odor of ammonia was produced (!).

Hydrolysis of the acyl chloride of α-chloroisovalerohydroxamic acid. 2.2 g of the substance was heated on a water bath for 18 hours with 70 ml of water. The substance dissolved almost completely. The aqueous so-

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* An aqueous solution of hydrogen chloride with an admixture of ether.

lution contained 0.7897 g of hydrogen chloride. The hydrolysis of one atom of chlorine must give 0.472 g of HCl, two atoms would give 0.944 g HCl. The percentage of hydrolysis (calculated for 2 atoms of chlorine) was 83.6.

1.26 g of a viscous colorless liquid, which crystallized, was extracted from the aqueous solution with ether. After it had been dried on a porous plate the m. p. was 82-84°. According to data [11], the m. p. of α-hydroxy-isovaleri acid is 86°.

Found %: neutralization equiv. 120.6. C_4H_9OCOOH. Calculated %: neutralization equiv. 118.1.

The reaction of nitrosyl chloride with 1-butene in the presence of hydrogen chloride. 51 g of 1-butene, cooled to -50°, and 112 g of nitrosyl chloride (-50°) were added to a solution of 20 g of hydrogen chloride in 700 ml of anhydrous ether, cooled to -12°. The red-brown mixture was poured into 13 ampoules, cooled with ice and salt. The ampoules were plugged with cotton wool and were left in a cooling mixture. The next day the temperature of the bath was +20°, the red tinge of the reaction mixture had disappeared and it now had a greenish tinge. The volume of the liquid in all the ampoules was somewhat reduced as a result of the volatiliza-tion of part of the hydrocarbon and nitrosyl chloride and a small layer of a transparent yellowish liquid was pres-ent on the bottom of the ampoules. Of the 13 ampoules 10 were sealed and 3 were left open. After a day in the sealed ampoules the color of the liquid was already darker (brown) and the volume of the lower layer was some-what reduced. When the ampoules were opened a slight pressure was observed after they had been cooled. In the three unsealed ampoules the volume again showed a reduction (2-3 ml) and the color of the liquid was dark orange. The ethereal solution was separated from the lower layer, the total volume of the lower layer was 12 ml, after the addition of water an ethereal layer of 5 ml came to the top; 7 ml of water was, therefore, liber-ated during the reaction. The brown ethereal solution was washed with four lots of water (total 500 ml), brown fumes of nitrogen dioxide, formed by the hydrolysis of the unreacted nitrosyl chloride, being given off. The pale-green ethereal solution was washed twice with a 5% solution of sodium bicarbonate (200 ml) and twice with water (200 ml); it was dried with anhydrous sodium sulfate. The ether, hydrocarbon and highly volatile fractions were distilled under vacuum and collected in a trap (-50°). The dirty-green residue was distilled under vacuum in a current of nitrogen.

After the ether had been driven off and the residue distilled under vacuum, 5.9 g of 1,2-dichlorobutane was obtained from the liquid retained in the traps; the b. p. was 41-43° at 40 mm, d^{20}_4 1.1178, $n^{20}D$ 1.4444 (accord-ing to data [12]; b. p. 31° at 28 mm, d_4^{20} 1.1187, $n^{20}D$ 1.440).

When the main part of the reaction products was distilled, 43.0 g of the acyl chloride of α-chloro-N-butyr-ohydroxamic acid, with a b. p. of 67-70° at 3 mm, was obtained. After several distillations under vacuum the following fractions were obtained: 1st, b. p. 58-59° at 2 mm, 13.5 g; 2nd, b. p. 59° at 2 mm, 11.3 g.

For 1st fraction: d_4^{20} 1.2970, $n^{20}D$ 1.4894, MR_D 34.75; calc. 34.73.

Found %: Cl 44.35° (Korshun). $C_4H_7ONCl_2$. Calculated %: Cl 45.5.

For 2nd fraction: d_4^{20} 1.2957, $n^{20}D$ 1.4912, MR_D 34.89; calc. 34.73.

Found %: Cl 44.27. $C_4H_7ONCl_2$. Calculated %: Cl 45.5.

Both fractions were colorless transparent liquids, soluble in ether and other organic solvents. They were slowly decomposed by water in the cold and rapidly decomposed when heated. The aqueous solution had an acid reaction, gave a reaction for chlorine ions and a reaction for hydroxamic acid with a solution of ferric chlo-ride (dark-red coloration) and after long standing of the substance with water, the aqueous solution reduced Fehl-ing solution.

The acyl chloride of α-chlorobutyrohydroxamic acid decomposed still more readily than the acyl chloride of α-chloroisovalerohydroxamic acid. When the substance was kept in a sealed vessel, colorless crystals, mainly hydroxylamine hydrochloride, were deposited by the next day.

Hydrolysis of the acyl chloride of α-chlorobutyrohydroxamic acid. 3 g of the substance was heated with 50 ml of water on a water bath for 2.5 hours, the major part of the oil dissolving. The aqueous solution had an acid did not give a qualitative reaction for hydroxamic acid with a solution of ferric chloride. The aqueous solution

* The analysis gives a low value for the chlorine content because of the rapid decomposition of the substance.

was extracted for 14 hours in an extractor with ether; after the ether had been driven off and the residue distilled, α-hydroxybutyric acid was obtained in the form of a viscous colorless liquid, the weight being 0.9 g; it was re-crystallized in a vacuum desiccator over phosphorus pentoxide. The m. p. was 39-40° (according to data [13]: m. p. 43-44°). α-Hydroxybutyric acid, with an m. p. of 41-42.5°, was obtained from the aqueous solution by hy-drolysis in the cold (for several days).

Found %: neutralization equiv. 105.6. $C_3H_7O(COOH)$. Calculated: neutralization equiv. 104.1.

The reaction of 4-nitro-3-chloro-2-methylbutane with hydrogen chloride in ethereal solution. 5.0 g of the nitrochloro compound (b. p. 54-55° at 2 mm, $n^{20}D$ 1.4544) were dissolved in 40 ml of anhydrous ether, con-taining 2.8 g of hydrogen chloride and were left in a sealed ampoule at room temperature. After 7 days the am-poule was opened and the ether was washed out from the hydrogen chloride by shaking with water; after the liq-uid had been dried by sodium sulfate, the ether was driven off and the residue was distilled under vacuum. 4.2 g of nitrochloroisopentane, with a b. p. of 57-58° at 3 mm and $n^{20}D$ 1.4550, was obtained.

SUMMARY

1. When nitrosyl chloride reacts with 2-methyl-3-butene and 1-butene in a solution of ethyl ether in the presence of hydrogen chloride, approximately 50% yields of the acyl chlorides of α-chloroisovalerohydroxamic and α-chlorobutyrohydroxamic acids are obtained. This reaction is a new one and is evidently a general meth-od for obtaining the acyl chlorides of α-chlorohydroxamic acids from monosubstituted ethylenes.

Together with the acyl chlorides of α-chlorohydroxamic acids the reaction gives small amounts of saturated dichlorides, 3,4-dichloro-2-methylbutane and 1,2-dichlorobutane, and in the reaction with 2-methyl-3-butene , 4-nitro-3-chloro-2-methylbutane is also obtained.

2. The formation of the acyl chlorides of α-chlorohydroxamic acids is caused by the presence of hydrogen chloride in the reaction medium. Under the influence of hydrogen chloride the primary reaction products, chlo-ronitroso compounds, undergo rearrangement into the oximes of α-chloroaldehydes, which with nitrosyl chloride give acyl chlorides of α-chlorohydroxamic acids.

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THE INVESTIGATION OF METHODS OF DISPLACEMENT OF HYDROGEN IN OXIDATION-REDUCTION REACTIONS

XI. THE REDUCTION OF BENZOPHENONE BY SODIUM ALKOXIDES AND ALUMINUM, AND ALCOHOLS AND SODIUM

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As a result of the investigation of the mechanism of oxidation-reduction reactions of organic compounds by means of deuterium it was established that the hydrogen from the C-H bonds of the reducing agents is transferred to the carbon atoms of the reduced compounds. The displacement of the hydrogen is not accompanied by its isotopic exchange with the medium [1]. In particular, this method of transfer of hydrogen is observed in all instances when alcohols or alcoholic solutions of alkoxides served as the reducing agents [2-4], for example, in the reduction of carbonyl compounds by alcohols in the presence of aluminum alkoxides [2].

It is known that alcoholic solutions of sodium alkoxides also act as a reducing medium. The conditions for reduction by aluminum and sodium alkoxides are essentially different because in the first case the reduction takes place in an acid medium, and in the second case in a strongly alkaline medium. In general, sodium alkoxides are less effective reducing agents for carbonyl compounds than aluminum alkoxides [18]; in certain instances, however, when the use of aluminum alkoxides does not give the desired result the reduction can be carried out with sodium alkoxide [10]. From this it follows that there is a qualitative difference as well as a quantitative one between the behavior of aluminum and sodium alkoxides. The sum total of our previous data makes it possible to assume, however, that both processes are analogous as regards sources and method of transfer of hydrogen.

The object of the present investigation was the experimental confirmation of this assumption and the elucidation of the role of the hydrogen of the C-H bonds of alcohols (or alkoxides) during reduction by alcohols and metallic sodium.* * In addition, because of considerations given below, we determined the value of the kinetic isotopic effect in the Meerwein-Ponndorf-Verley reaction.

We decided on the reduction of benzophenone by N-butyl, isoamyl and ethyl alcohols in the presence of the corresponding sodium alkoxides on the one hand and butyl and ethyl alcohols and sodium on the other [6,7] as the subject to be investigated.

In the first series of experiments we investigated the reduction of benzophenone by solutions of sodium alkoxides in alcohols containing deuterium in the hydroxyl group. The experiments were carried out in the following manner : 0.1-0.2 g-at. of metallic sodium was dissolved with boiling in 0.2-0.6 mole of heavy alcohol (this took 1.5-2 hours); 0.04-0.05 mole of benzophenone was added to the solution obtained and heating was continued at 140° for a further 30 minutes. The benzhydrol formed was separated from the reaction mixture and after it had been cooled and neutralized it was steam distilled or extracted with ether. In the latter case the deuterium from the benzhydrol hydroxyl group was washed out by dissolving it repeatedly in methyl alcohol
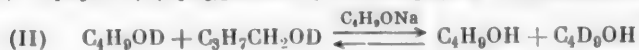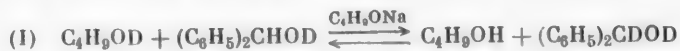
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* Deceased.

** In this case, after the first portions of sodium have been dissolved in the alcohol conditions of reduction by alcoholic solutions of sodium alkoxides are created in the reaction medium.

and evaporating the methanol solution. After it had been recrystallized from ligroin the benzhydrol had an m.p. of 67-68°. The yield was 90-95%. To determine the isotopic composition of the separated benzhydrol it was burnt over cupric oxide and its deuterium content was determined from the density of the water of combustion by the flotation method. The amounts of the substances used, the deuterium content in the hydroxyl of the initial alcohol and the results of the analysis of the water of combustion are given in Table 1. Column 6 of this table gives the deuterium content in the C-H bond of the carbinol group. The values in column 6 were obtained by multiplying the values of the excess density of the water of combustion of benzhydrol by 12, because as a result of combustion the hydrogen of the C-H bond of the carbinol,[*] group is diluted 12 times by the hydrogen from the other positions in the molecule.

TABLE 1

Reduction of Benzophenone by Sodium Butoxide, Isoamoxide and Ethoxide in the Corresponding Alcohols

Expt. No.	Amount of initial substances (in moles)			Deuterium content (in γ units)			Remarks
	$(C_6H_5)_2C=O$	alcohol	Na	In the O-H of the initial alcohol	H_2O of comb. $(C_6H_5)_2C=O$	In the C-H of the initial alcohol	
Reduction by sodium butoxide in C_4H_9OD						
1	0.055	0.65	0.22	23540	137	1640	The alcohol from
2	0.055	0.43	0.17	23540	135	1620	the reaction mix-
3	0.044	0.43	0.17	23540	122	1460	ture contained 650-
4	0.055	0.43	0.17	23540	122	1460	770 γ units of deuterium in the C-H bonds
5	0.055	0.42	0.17	23540	8	100	Experiments with light
6	0.027	0.13	0.076	23540	32	380	alkoxides
	Reduction by sodium isoamoxide in $(CH_3)_2CH_2CH_2CH_2O_3D$						
7	0.055	0.36	0.22	19600	100	1200	The alcohol from the reaction mixture contained 780 γ units of deuterium in the C-H bonds.
8	0.044	0.36	0.22	19600	109	1310	
	Reduction by sodium ethoxide in C_2H_5OD						
9	0.03	0.51	0.21	9240	149	1790	130°, 40 ml of
10	0.055	0.10	0.10	9410	23	280	xylene with light alkoxide

(I) $C_4H_9OD + (C_6H_5)_2CHOD \xrightleftharpoons{C_4H_9ONa} C_4H_9OH + (C_6H_5)_2CDOD$

(II) $C_4H_9OD + C_3H_7CH_2OD \xrightleftharpoons{C_4H_9ONa} C_4H_9OH + C_4D_9OH$

Reduction with butyl[*] and isoamyl alcohols was carried out at 140° in a thermostat (except for experiments 1 and 2 in which the reaction was carried out with boiling on a sand bath; the temperature of the liquid phase during the boiling of the mixture varied between 135 and 142°). Preliminary experiments on reduction by sodium ethoxide in ethyl alcohol showed that when the mixture was boiled for a considerable time (1.5-2.5 hours) reduction does not take place; here, the temperature of the liquid phase reached 80-85°. It was only possible to reduce benzophenone to benzhydrol with sodium ethoxide by adding 50 ml of xylene to the reaction mixture and thus increasing the boiling point to 125-130°.

[*][Carbinol = α carbon atom. Translator's note].

[**]Preliminary experiments on the reduction of benzophenone by sodium butoxide were carried out by L. Bel'mas, a student at the Dnepropetrovsk State University.

The data given in Table 1 (experiments 1-4, 7-9) show that when benzophenone is reduced by sodium butoxide and isoamoxide a considerable amount of deuterium is transferred to the benzhydrol. The deuterium content in the carbinol group of benzhydrol is, however, 1/10 less than its content in the hydroxyl of the initial alcohol. We assumed that deuterium enters the benzhydrol molecule not as a result of the reduction reaction but owing to the exchange, proceeding simultaneously, between the hydrogen of the hydroxyl groups of the alcohol, on the one hand, and the hydrogen of the C-H bonds of benzhydrol (I) and the alkyl radicals of the alcohols (and alkoxides) themselves, on the other (II).

In actual fact, it was found that when ordinary benzhydrol is heated in a solution of sodium butoxide in heavy butyl alcohol under conditions similar to those for the reduction of benzophenone, exchange takes place. After 30 minutes exchange we found 700 γ units of deuterium (the mean of 3 experiments) in the C-H bonds of benzhydrol. The initial alcohol and the ratio of the amounts of alcohol and sodium in the exchange experiments were the same as in experiments 2-4. When benzhydrol was heated for 2 hours under the same conditions 1200-1300 γ units of deuterium were found in it. The oxidation of a mixed sample of benzhydrol, obtained in experiments 1-4, to benzophenone and the isotopic analysis of this benzophenone showed that only the hydrogen of the C-H bonds of the carbinol group takes part in the exchange because the benzophenone hardly contained deuterium. In addition, it was found that after the removal of the deuterium from the hydroxyl group, the alcohol from the reaction mixture in the reduction experiments contains considerable amounts of deuterium, as in the case of the alcohol after sodium had been dissolved in it. The oxidation of these samples of alcohols to butyric acid and the isotopic analysis of the latter showed that the deuterium content in the α-position of the alcohol hardly differs from its content in the other positions of the alkyl radical of the alcohol and corresponds to 650-770 γ units.

The experimental data confirm, therefore, that when alcoholic solutions of sodium alkoxides are boiled, exchange processes, according to systems (I) and (II), take place at the same time as the reduction of benzophenone. The fact that the deuterium content in the C-H bonds of benzhydrol is similar to the total amount of deuterium entering the alkyl radicals of the alcohol and into the carbinol group of benzhydrol as a result of exchange (700 γ + 700 γ = 1400γ) is an indication in favor of our initial assumption, i.e. it indicates the selective transfer of hydrogen from the C—H bonds of the alcohols (or alkoxides) to the carbonyl atom of benzhydrol when it is reduced. The exchange reaction takes place far more slowly than the reduction: after 2 hours at 140° the exchange of hydrogen between the hydroxyl group of butyl alcohol and its alkyl radicals is only 30%, whereas reduction is completed in 30 minutes. It was, therefore, possible for us to confirm this assumption by a more direct method.

In experiments 5,6 and 10 the reduction of benzophenone was carried out by alkoxides, prepared from ordinary alcohol, and dissolved in alcohols containing deuterium in the hydroxyl group. By this method we eliminated protracted heating of solutions of sodium in heavy alcohol during the preparation of solutions of alkoxides, a process which leads to the introduction of deuterium in the C-H bonds of the alkyl radicals of the alcohols.
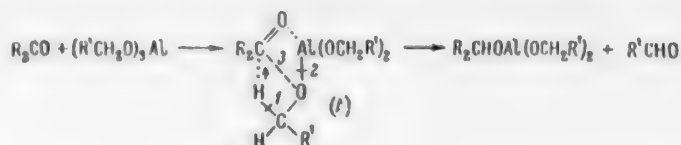
The benzhydrol obtained in experiments 5,6 and 10 contained only a slight amount of deuterium. This definitely proves that hydrogen is transferred directly from the C—H bonds of the alcohol to the carbinol atom of benzophenone.

With respect to the mechanism of the transfer of hydrogen, reduction by alcoholic solutions of sodium alkoxides is, therefore, analogous to reduction by aluminum alkoxides and can be expressed by the system

$$R_2C{=}O \;+\; R'CH_2OD \xrightarrow{\;R'CH_2ONa\;} R_2CHOD + R'CHO$$
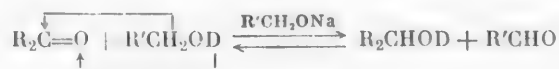
According to present opinions the particular features of the Meerwein-Ponndorf-Verley reaction, namely its specific character, its stereospecific character and the direct transfer of hydrogen from the C-H bonds of the reducing agent to the carbonyl atom of carbon without the participation of the solvent is explained

by the fact that the reaction takes place via a cyclic transition complex (A) [8,9], obtained as a result of the tendency of aluminum alkoxides to form coordination compounds with carbonyl compounds*

$$R_2CO + (R'CH_2O)_3Al \longrightarrow R_2C\underset{\substack{\displaystyle :\ :\\ H\ \ I\ \ O\\ \diagdown C \diagup\\ H \diagup \diagdown R'}}{\overset{\substack{O\\ \|\\ 3}}{\longrightarrow}}Al(OCH_2R')_2 \longrightarrow R_2CHOAl(OCH_2R')_2 + R'CHO$$

It is not difficult to imagine a similar transition complex in the case of reduction by sodium alkoxides (B), also. Here the formation of a complex is due to the electrostatic reaction of the polarized bonds $C^{\delta+} + O^{\delta-}$ and $O^{\delta-} - Na^{\delta+}$.
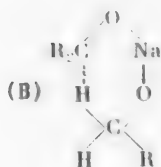
One of us previously advanced the suggestion that low values of the kinetic isotopic effect [11, 12] are characteristic for the transfer of hydrogen to cyclic transition complexes like (A) and (B). It was of interest to check this suggestion by the example of the Meerwein-Ponndorf-Verley reaction, for which the formation of a transition complex (A) is well-founded [8, 9, 10]. We carried out the reduction of benzophenone and benzaldehyde by heavy aluminum isopropoxide [$(CD_3)_2CDO]_3Al$ in an excess of heavy isopropyl alcohol and determined the value of the isotopic effect from the composition of the reduction products of benzhydrol and benzyl alcohol.

The experiments were carried out according to the method described in Wilde's review of this subject [5]. The amounts of the substances used, the isotopic composition of the initial alcohol, alkoxide and reduction products and also the values $\alpha = k_H / k_D$ found for the kinetic isotopic effect are given in Table 2. α was calculated according to the formula $\alpha = \dfrac{\ln(1-S)}{\ln\left(1-S\dfrac{y}{x}\right)}$ [13], where S is the molar ratio of the amounts of the carbonyl compound to the total amount of alcohol and alkoxide, x and y are the contents of deuterium in the initial isopropyl alcohol and in the C–H carbinol group of the reduction products, respectively.

Heavy isopropyl alcohol was obtained by the action of metallic sodium on a mixture of equal volumes of D_2O, ether and acetone [25]. The deuterium from the hydroxyl group was removed by repeated washing with a saturated aqueous solution of potash, after which the alcohol was dried and distilled. The b.p. was 81-82.5°, n_D^{20} 1.3780.

The oxidation of the samples of aluminum isopropoxide, obtained from this alcohol, to acetone and the isotopic analysis of this acetone showed that the deuterium in it was uniformly distributed in all seven positions. The aluminum isopropoxide was prepared in the manner described in [5].

The results of the above-mentioned experiments show that the reduction of benzophenone and benzaldehyde by aluminum isopropoxide in isopropyl alcohol takes place with a slight isotopic effect $k_H / k_D = 1.8-1.9$, close to the value found by us previously for the Leukart [11] and Cannizzaro [16] reactions. The data obtained confirm the assumption that the intramolecular transfer of hydrogen to the cyclic complexes is accompanied by a comparatively small isotopic effect. The data of Dunn and Warkentin [17], who determined the value of the isotopic effect in the reduction of benzophenone by magnesium isobutyl bromide, are also in favor of this assumption. As far back as 1942 Whitmore [20] sugested the formation of a cyclic transition complex C similar in structure to (A), for this reaction.

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*In our first work dealing with the mechanism of the Meerwein-Ponndorf-Verley reaction [2] we assumed the intermediate formation of a semi-acetal and the intramolecular transfer of hydrogen in it. The transfer of hydrogen (A) is better-founded, both from the energy aspect [19] and general chemical premises [11]. This does not exclude the possibility of the formation of a semi-acetal. In point of fact, as a result of the rupture of bonds 1 and 2 and the formation of bond 4 the complex (A) decomposes into the reaction products, bond 2 is ruptured and the formation of bond 3 converts it to a semi-acetal.
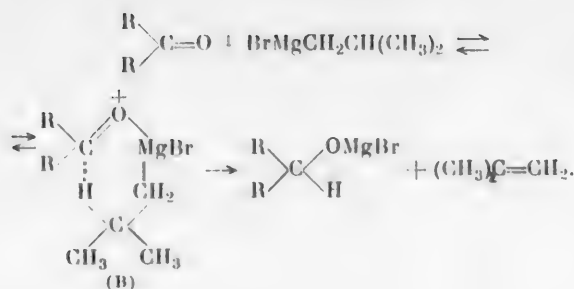
$$\begin{array}{c} R \\ R \end{array}\!\!>\!\!C\!\!=\!\!O + BrMgCH_2CH(CH_3)_2 \rightleftarrows$$

$$\rightleftarrows \quad \begin{array}{c} R \\ R \end{array}\!\!>\!\!C \cdots \begin{array}{c} \overset{+}{O} \\ | \end{array} MgBr \longrightarrow \begin{array}{c} R \\ R \end{array}\!\!>\!\!C \begin{array}{c} OMgBr \\ H \end{array} + (CH_3)_2C\!\!=\!\!CH_2.$$

(B)

TABLE 2

Reduction of Benzophenone and Benzaldehyde by Aluminum Isopropoxide in Isopropyl Alcohol

Carbonyl compound	Amount of initial substance (in mole)			Solvent (ml)	Deuterium content (in γ units)			$\dfrac{k_H}{k_D} = \alpha$	
	$\begin{array}{c}R\\R\end{array}\!>\!C\!=\!O$	Isopropyl alcohol	Aluminum isopropoxide		In the α-C–H of the alcohol and alkoxide	In the water of combustion	In the C–H of the alcohol group		
$(C_6H_5)_2CO$	0.03	0.39	0.025	—	4000	188	2260	1.83	Mean 1.79
	0.027	0.39	0.025	—	4000	177	2120	1.89	
	0.027	0.39	0.025	—	4000	190	2280	1.66	
C_6H_5CHO	0.066	0.194	0.015	CCl$_4$ (50)	4000	269	2150	2.01	Mean 1.95
	0.066	0.194	0.015		4000	282	2260	1.90	
	0.066	0.194	0.015		4000	276	2210	1.94	

The value of the isotopic effect, found by Dunn and Warkentin, was 2.0-2.2. The authors [17] explained the low value of the isotopic effect by the commensurate values of the rates of decomposition of C in the forward and reverse directions. *A similar explanation is also possible for the low values we found for the isotopic effect. Comparing the results of our experiments with the data of Dunn and Warkentin it is difficult to imagine, however, that in three different instances (under different conditions) with the participation of different reagents the ratio of the decomposition rates of the intermediate complex in the forward and reverse directions remained almost unchanged. These considerations make the explanation of the authors [17] of little likelihood and justify the preference for our explanation of the low value of the isotopic effect.

From our data it also follows that the splitting off of hydrogen from the molecules of the reducing agent takes place in the stage determining the rate of the process.

In the case of the reduction of benzophenone by sodium alkoxide the determination of the isotopic effect was complicated by the exchange process taking place at the same time. The fact that in the experiments on reduction by alkoxides with deuterium in the C-D bonds the deuterium content in the reduction product was very close to its total content in the alkoxide and in the benzhydrol after exchange indicates that the isotopic effect was either absent or of low value.

Being convinced by the results of the 1st series of experiments that during reduction by sodium alkoxides only the hydrogen of the C–H bonds of the reducing agent is transferred to the carbonyl atom of benzophenone, without the solvent participating, in this transfer, we turned to the elucidation of the role of this process in reduction by alcohols and sodium.

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*For a kinetic analysis substantiating this hypothesis see [26].

TABLE 3
Reduction of Benzophenone by Alcohols and Sodium

Expt. No.	Amounts of initial substances (in mole)			Tempera-ture	Solvent (ml)	Deuterium content (in γ units)			Percentage of transfer of D	Reduction product
	$(C_6H_5)_2C=O$	Alcohol	Na			In the hydroxyl of the initial alcohol	In the water of combustion of the reduction product	In the C–H of the carbinol or methylene group		

Reduction in ethyl alcohol.

1	0.055	1.74	0.43	80	—	9240	1083	6500	} 70	} $(C_6H_5)_2CH_2$
2	0.055	1.74	0.43	80	—	9240	1076	6450		
3	0.030	0.51	0.21	95—100	} Xylene (20)	9240	1248	7490	} 80	
4	0.030	0.51	0.21	95—100		9240	1227	7360		
5	0.049	0.17	0.07	125—133	Xylene (80)	9240	113	1360	15	$(C_6H_5)_2CHOH$

Reduction in butyl alcohol.

6	0.055	0.43	0.22	135—140	—	23360	431	5170	22	} $(C_6H_5)_2CHOH$
7	0.034	0.21	0.16	135—140	—	23360	421	5050	21	
8	0.055	0.43	0.17	135—140	—	25770	446	5350	21	
9	0.055	0.43	0.17	100	—	23540	628	7560	32	
10	0.055	0.43	0.17	100—120	—	25770	727	8720	34	

The experiments were carried out in the following manner. Small lumps of metallic sodium were added gradually to boiling solutions of benzophenone in heavy alcohols $RCH_2OD(R=CH_3$ and $C_3H_7)$. It took 1.5-2 hours for 4-5 g of sodium to dissolve in butyl alcohol. It dissolved more quickly in ethanol. The details and the results of these experiments are given in Table 3. Column 9 of this table gives the values of the ratio of the deuterium content in the hydroxyl of the initial alcohol and the C–H bonds of the benzhydrol carbinol group, or in the methylene group of diphenylmethane, expressed as percentages. We call these values the percentage of transfer of deuterium to the reduction product.
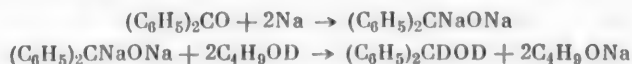
According to the data of Klages and Allendorf [14], benzophenone is smoothly reduced by boiling ethyl alcohol and sodium to diphenylmethane. According to our data (see above), reduction by sodium ethoxide takes place only at a higher temperature, giving benzhydrol. A comparison of these facts indicates a difference in the course of both processes and, in particular, makes it possible to conclude that under the usual conditions of reduction by ethyl alcohol and sodium at 80° hydrogen is not transferred from the C–H bonds of the alcohol (or alkoxide). In accordance with this, as a result of reduction by heavy ethyl alcohol C_2H_5OD and sodium at 80° and at 95-100° in xylene we obtained heavy diphenylmethane. The deuterium content in its methylene group corresponded to 0.7-0.8 of the deuterium content in the hydroxyl of the initial alcohol (experiments 1-4, Table 3). When we repeated these experiments in a mixture of alcohol and xylene at a higher temperature (125-133°), instead of diphenylmethane we obtained benzhydrol containing slightly more than 1/7th of the deuterium in the initial heavy alcohol (experiment 5, Table 3) and with almost the same content as the benzhydrol obtained by reduction with sodium ethoxide (experiment 9, Table 1). From this it follows that in reduction by ethyl alcohol and sodium at 130° the transfer of hydrogen from the C–H bonds of the reducing agent, not from its hydroxyl groups, plays the predominant role. The introduction of small amounts of deuterium into the molecules of the deuterium formed should evidently be attributed to exchange taking place at the same time.

In contrast to its reduction in ethyl alcohol, when benzophenone was reduced by sodium in butyl alcohol it was found that at 100°, as at 140°, the reaction product was benzhydrol. The higher the reaction temperature, the less deuterium it contained. The benzhydrol obtained at 140°, i.e. under conditions similar to those for reduction by sodium butoxide was nevertheless far heavier than in reduction by alkoxide (5000 γ units of deuterium in the C–H bonds of the carbinol group instead of 1400-1600 γ units). The introduction of such a large amount

of deuterium cannot be explained by exchange alone. Neither can it be explained by the transfer of hydrogen from only the hydroxyl groups of the alcohol with an isotopic effect of $\dfrac{k_H}{k_D}$ = 3-4, because in this case the amount of deuterium transferred to the benzhydrol must have increased with reduction in temperature, whereas it is known that the isotopic effect increases with reduction in temperature.

The data obtained during reduction in butyl alcohol must evidently be explained by the parallel course of two processes, reduction by alkoxide and metallic sodium. The first process leads to the transfer of hydrogen from the C—H bonds of the reducing agent to the benzhydrol, while the second leads to the transfer of hydrogen from the hydroxyl groups of the alcohol. The ratio of the rates of both processes depends on the temperature and the chemical nature of the alcohol. The influence of temperature is clearly evident from the results of experiments in ethyl alcohol whereas the influence of the chemical structure of the alcohol is shown by a comparison of the results of reduction at 100° in ethyl and butyl alcohols.

The formation of one or another product during reduction by metallic sodium (depending on whether the reaction is carried out in ethyl or butyl alcohol) can be tentatively explained on the basis of the existing theory of the reduction of organic compounds by metals [21, 22, 23] and the differences in the rates of reaction of sodium with benzophenone and alcohols. It is known that benzophenone can react with sodium, forming very reactive sodium ketyls [24]. It is also known that sodium reacts with ethyl alcohol far more rapidly than with butyl alcohol. It may be considered that the reaction of sodium with alcohol predominates during reduction in ethyl alcohol. At 80° and 100° the reaction proceeds as a catalytic hydrogenation of benzophenone on the surface of the metal [23] with the formation of diphenylmethane. At a higher temperature (130°) the period for which the hydrogen remains on the metal is reduced to such an extent that catalytic hydrogenation does not have time to take place but, on the other hand, sodium ethoxide, which reduces the benzophenone to benzhydrol (see system B), rapidly accumulates in the reaction mixture. During reduction in butyl alcohol the rates of reaction of sodium with the alcohol and ketone are commensurate. Reduction by sodium takes place via the formation of a sodium ketyl according to Wilstatter's mechanism [15,22] and not by catalytic hydrogenation

$$(C_6H_5)_2CO + 2Na \rightarrow (C_6H_5)_2CNaONa$$
$$(C_6H_5)_2CNaONa + 2C_4H_9OD \rightarrow (C_6H_5)_2CDOD + 2C_4H_9ONa$$

The reduction product is, therefore, not diphenylmethane but benzhydrol. Reduction by sodium butoxide according to system (B) takes place simultaneously with the formation of "light" benzhydrol. The ratio of the rates of these two processes is determined by the temperature: the lower the temperature, the lesser the degree of participation of sodium butoxide and the heavier the benzhydrol formed.

In conclusion it is interesting to note that a number of empirical laws recommended for increasing yields during reduction by the Bouveault-Blanc method [7], namely the continued heating of the reaction mixture after the sodium has completely dissolved, the addition of xylene to the reaction mixture and the substitution of butyl for ethyl alcohol are given a rational explanation in the light of the results of our experiments, which have shown the role of sodium alkoxide in reduction by alcohols and sodium.

SUMMARY

1. The mechanism of the reduction of benzophenone by sodium butoxide, isoamoxide and ethoxide in solutions of the corresponding alcohols, labelled with deuterium in the hydroxyl group, and also by heavy ethyl alcohol (C_2H_5OD) and butyl alcohol (C_4H_9OD) and sodium was investigated.

2. Reduction with sodium ethoxide takes place in a similar manner to reduction by aluminum alkoxide, i.e. hydrogen from the C—H bonds of the alcohol or alkoxide is selectively transferred to the carboxyl atom of the carbon of benzophenone.

3. Reduction by alkoxides can also play a significant role in reduction by alcohols and sodium. The proportionate role played by both methods during reduction by sodium in ethyl alcohol depends on the temperature. At 80-100° the reduction product is diphenylmethane. It is formed by the hydrogen of the hydroxyl groups of the alcohol. At 125-130° benzhydrol is formed and hydrogen is preferentially transferred from the C—H bonds of the alcohol or alkoxide.

4. During reduction by sodium in butyl alcohol at 100 and 140° only benzhydrol is formed, its isotopic composition indicating the parallel course of both processes.

5. The data obtained are explained on the basis of the contemporary theory of reduction by metals.

6. The kinetic isotopic effect during the reduction of benzophenone and benzaldehyde by isopropyl alcohol in the presence of aluminum isopropoxide $(CD_3)_2CDOH + [(CD_3)_2CDO]_3Al$ was determined, the values being 1.8 and 1.9, respectively. These data confirm the assumption that low values of the isotopic effect are characteristic for the intramolecular transfer of hydrogen to cyclic transition complexes.

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THE SYNTHESIS OF DERIVATIVES OF PHENYLTRIFLUOROMETHYL-SULFONE

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The object of the present work was to obtain semiproducts for the synthesis of azo and cyanine dyes containing a trifluoromethylsulfonyl group.

3-Amino -4-fluoro- and 3-amino-4-chlorophenyltrifluoromethylsulfones were obtained according to the following system


Hal=F or Cl.
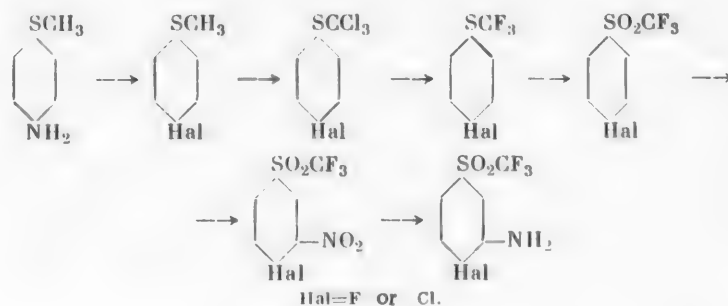
3-Nitro-4-methoxyphenyltrifluoromethylsulfone was obtained by the action of sodium methoxide on 3-nitro-4-chlorophenyltrifluoromethylsulfone and was then reduced to the amine (A).

(A)
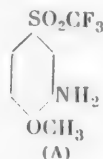
In addition to the above-mentioned compounds we also synthesized 2-methyl-6-trifluoromethylsulfonyl-benzimidazole, 2-methyl-3-phenyl-6-trifluoromethylsulfonylbenzimidazole and 2-methyl-5-trifluoromethyl-sulfonylbenzothiazole according to the system on the following page.

The latter base was converted to the quaternary salt, from which carbocyanine and the styryl dye were obtained. Like other electronegative substitutents — NO_2 [1], CF_3 [2] — in the 5 position of the benzothiazole ring the CF_3SO_2 group hardly changes the absorption maximum of thiacarbocyanine. In the styryl dye the CF_3SO_2 group displaces the absorption maxima 25 mμ towards the long waves(see table). 3-Nitro-4-hydrazinophenyl-trifluoromethylsulfone was also obtained.

R=H or C₆H₅
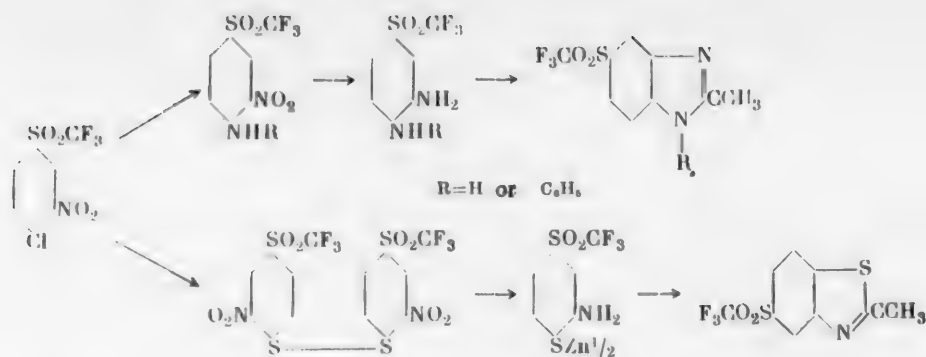
Formula of the dye	λ_{max} (in m μ)	
	5-sub-stituted	Dyes with-out SO_2CF_3
I	556	558
I	555	530

EXPERIMENTAL

p-Chlorophenylmethylsulfide was obtained by replacing the amino group in p-aminophenylmethylsulfide [3] by chlorine by the Sandmeyer reaction. The yield was 67%. The b.p. was 228-229°, or 104-105° at 10 mm. According to literature data the b.p. is 172° [4,5] and 231° [6]. In the latter case the p-chloromethylsulfide was obtained by methylating p-chlorothiophenol.

Found %: S 19.90, 20.05. C_7H_7SCl. Calculated %: S 20.18.

p-Chlorophenyltrichloromethylsulfide. 64.8 g of p-chlorophenylmethylsulfide was dissolved in 250 ml of dry chloroform, cooled with ice water and dry chlorine was passed through the solution, exposed to an electric light, until the theoretical increase in weight had been attained. It was left for one hour at room temperature. The chloroform was distilled. The product crystallized out. The yield was 96 g (90%). After crystallization from petroleum ether the m.p. was 59-60°. (The compound is mentioned in the patent [7]).

Found %: Cl 53.95, 54.01. $C_7H_4SCl_4$. Calculated %: Cl 54.19.

p-Chlorophenyltrifluoromethylsulfide. A mixture of 80 g of p-chlorophenyltrichloromethylsulfide and 62 g of sublimated antimony trifluoride was heated until a reaction commenced. The product was distilled off, dissolved in ether and washed free from antimony trifluoride with 6N HCl. The yield was 46 g (71%). The b.p. was 173-174°, coinciding with that given in the patent [8].

p-Chlorophenyltrifluoromethylsulfone. 19 g of p-chlorophenyltrifluoromethylsulfide was added to a solution of 36 g of chromic anhydride in 80 ml of acetic acid; the mixture was heated with a reflux condenser for 3 hours on a water bath and boiled for six hours on a grid. The product was steam distilled, filtered and crystallized form methyl alcohol. The yield was 19 g (94%). The m.p. was 55-56°, coinciding with that given in the patent [8].

3-Nitro-4-chlorophenyltrifluoromethylsulfone   33 g of p-chlorophenyltrifluoromethylsulfone was added at 50-55° in small portions and with vigorous stirring to a nitrating mixture (13 ml of nitric acid (d 1.5), 20 ml of H_2SO_4 (d 1.84) and 22 g of 62% oleum); the temperature was raised over a period of 1 hour to 90-95° and maintained at this temperature for 1 hour. The mixture was poured onto ice. The product was filtered and crystallized from methyl alcohol. The yield was 33 g (84%). The m.p. was 55-56°.

Found %: N 4.65, 4.75. $C_7H_3O_4NSClF_3$. Calculated %: N 4.84.

3-Nitro-4-hydrazinophenyltrifluoromethylsulfone. 1. 4 g of hydrazine hydrate was added to a solution of 2 g of 3-nitro-4-chlorophenyltrifluoromethylsulfone in 12 ml of alcohol. The mixture became warm. The next day the product was filtered and crystallized from aqueous alcohol. The yield was 2 g (95%). The m.p. was 139-140°.

Found %: N 14.72, 14.83. $C_7H_6O_4N_3SF_3$. Calculated %: N 14.73.

3-Amino-4-chlorophenyltrifluoromethylsulfone. 5 g of 3-nitro-4-chlorophenyltrifluoromethylsulfone was dissolved in 25 ml of methyl alcohol and heated with a solution of 15 g of stannous chloride in 21 ml of concentrated hydrochloric acid for 2 hours on water bath. The yield was 3.8 g (84%). After crystallization from alcohol the m.p. was 94-95°.

Found %: N 5.58, 5.66. $C_7H_5O_2NSClF_3$. Calculated %: N 5.38.

The acetyl derivative melted at 115-116°.

Found %: N 4.44, 4.48. $C_9H_7O_3NSClF_3$. Calculated %: N 4.64.

p-Fluoromethylphenylsulfide. 30 g of p-aminophenylmethylsulfide was mixed with 70 ml of concentrated hydrochloric acid and cooled to 0°; 100 g of ice was added and the mixture was diazotized with a solution of 18 g of sodium nitrite in 36 ml of water. Diazonium borofluoride was precipitated by the addition of borofluoric acid, prepared from 53.4 g of boric acid and 175 g of 40% hydrofluoric acid. The precipitated diazonium borofluoride was filtered, dried and decomposed. The product was steam distilled, extracted with ether and distilled.   The yield was 18 g (60%). The b.p. was 184-185°.

Found %: S 22.31, 22.36. C_7H_7SF. Calculated %: S 22.53.

The product is described in literature [9]. It was obtained by methylating p-fluorothiolphenol. Its b.p. is given as 74° at 10 mm. An analysis was not carried out.

p-Fluorophenyltrichloromethylsulfide. This was obtained in a similar manner to p-chlorophenyltrichloromethylsulfide. The yield was 90% The b.p. was 107-108° at 6 mm. The compound is mentioned in the patent [7]. Its b.p. is given as 122° at 18 mm.

Found %:   S 13.01, 13.42. $C_7H_4SCl_3F$. Calculated %: S 13.2.

p-Fluorophenyltrifluoromethylsulfide. This was obtained in a similar manner to p-chlorophenyltrifluoromethylsulfide. The yield was 75.5% The b.p. was 138°.

Found %: S 16.38, 16.41. $C_7H_4SF_4$. Calculated %: S 16.32.

p-Fluorophenyltrifluoromethylsulfone. This was obtained in a similar manner to p-chlorophenyltrifluoromethylsulfone. The yield was 90%. The b.p. was 196-197°, the m.p. was 32°.

Found %: S 13.71, 13.84. $C_7H_4O_2SF_4$. Calculated %:   S 14.03.

3-Nitro-4-fluorophenyltrifluoromethylsulfone. This was obtained in a similar manner to 3-nitro-4-chlorophenyltrifluoromethylsulfone. The yield was 78% The b.p. was 133-135° at 8 mm.

Found %: N 4.99, 5.01. $C_7H_5O_4NSF_4$ Calculated %: N 5.12.

3-Amino-4-fluorophenyltrifluoromethylsulfone. This was obtained in a similar manner to 3-amino-4-chlorophenyltrifluoromethylsulfone. The yield was 81%   The m.p. was 65-66°.

Found %: N 5.85, 5.94. $C_7H_5O_2NSF_4$ Calculated % N 5.76.

The acetyl derivative melted at 133-134°.

Found %: N 5.13, 5.21. $C_9H_7O_3NSF_4$ Calculated %: N 4.94.

3-Nitro-4-methoxyphenyltrifluoromethylsulfone. A solution of 5 g of 3-nitro-4-chlorophenyltrifluoromethylsulfone in 25 ml of anhydrous methyl alcohol was mixed with a solution of 0.4 g of sodium in 25 ml of methyl alcohol. The mixture was boiled for 2 hours. The alcohol was distilled. The product was poured into water, filtered and crystallized from alcohol. The yield was 4.6 g (92%). The m.p. was 81-82°.

Found %: N 5.10, 5.16. $C_8H_6O_5NSF_3$ Calculated %: N 4.91.

3-Amino-4-methoxyphenyltrifluoromethylsulfone. This was obtained by reduction of the nitro compound with stannous chloride. The yield was 91% The m.p. was 91-92°.

Found : %: N 5.62, 5.74. $C_8H_8O_3NSF_3$. Calculated %: N 5.49.

The acetyl derivative melted at 135-136°.

Found %: N 4.96, 4.97. $C_{10}H_{10}O_4NSF_3$. Calculated %: N 4.71.

3-Nitro-4-aminophenyltrifluoromethylsulfone. 8 g of 3-nitro-4-chlorophenyltrifluoromethylsulfone in 10 ml of 25% aqueous ammonia was heated for 6 hours at 140-145° and for 1 hour at 150-155°. The product was filtered. It was crystallized from a mixture of benzene and petroleum ether. The yield was 5.5 g (75%). The m.p. was 127-128°.

Found % N 10.33, 10.40. $C_7H_5O_4N_2SF_3$. Calculated %: N 10.37.

3-4-Diaminophenyltrifluoromethylsulfone. A solution of 4.7 g of 3-nitro-4-aminophenyltrifluoromethyl-sulfone in 25 ml of methyl alcohol was reduced with a solution of 15 g of stannous chloride in 22 ml of concentrated hydrochloric acid. The product was crystallized from petroleum ether. The yield was 3.9 g (92 %). The m.p. was 109-110°.

Found %: N 11.42, 11.34. $C_7H_7O_2N_2SF_3$ Calculated % : N 11.66.

5-Trifluoromethylsulfonylquinoxaline. A mixture of 0.3 g of 3,4-diaminophenyltrifluoromethylsulfone and 0.26 g of benzil was boiled in alcohol on a water bath for 1 hour. The precipitated product was crystallized from methyl alcohol. The yield was 0.44 g (86%). The m.p. was 144-145°.

Found %: N 6.69, 6.71. $C_{21}H_{13}O_2N_2SF_3$ Calculated %: N 6.73.

2-Methyl-6-trifluoromethylsulfonylbenzimidazole. 5.6 g of 3,4-diaminophenylmethylsulfone was mixed with 20 ml of 20% hydrochloric acid and 10 ml of acetic anhydride and boiled on a grid for 2 hours. The base was then precipitated with ammonia. It was crystallized from a mixture of benzene and methyl alcohol. The compound was dried under vacuum at 110°. The yield was 5 g (80%). The m.p. was 153° from benzene.

Found %: N 10.29, 10.31. $C_9H_7O_2N_2SF_3$ Calculated %: N 10.6.

2-Nitro-4-trifluoromethylsulfonyldiphenylamine. 6 g of 2-nitro-4-chlorophenyltrifluoromethylsulfone was mixed with 12 g of aniline and heated on an oil bath at 140-145° for 5 hours. After the mixture had cooled it was poured into 10% hydrochloric acid, the precipitate was filtered, washed with dilute hydrochloric acid and crystallized from methyl alcohol. The yield was 6.58 g (92%). The m.p. was 99-100°.

Found : N 7.98, 8.12. $C_{13}H_9O_4N_2SF_3$ Calculated %: N 8.09.

2-Amino-4-trifluoromethylsulfonyldiphenylamine. A solution of 6.58 g of 2-nitro-4-trifluoromethylsulfonyl-diphenylamine in 25 ml of alcohol was mixed with a solution of 15.8 g of stannous chloride in 15 ml of hydrochloric acid and boiled on a water bath for 3 hours. The yield was 5.45 g (90.5%). The m.p.   was 135-136°.

Found %: N 8.99, 9.10. $C_{13}H_{11}O_2N_2SF_3$. Calculated %: N 8.86.

2-Methyl-3-phenyl-6-trifluoromethylsulfonylbenzimidazole. A mixture of 2.5 g of 2-amino-4-trifluoro-methylsulfonyldiphenylamine, 1.2 ml of acetyl chloride and 10 ml of benzene was boiled for 6 hours. The precipitated product was filtered, dissolved in dilute hydrochloric acid and precipitated with ammonia. The yield was 2 g (74.3%). After crystallization from alcohol the m.p. was 190-191°.

Found %: N 7.98, 8.09. $C_{15}H_{11}O_2N_2SF_3$. Calculated %: N 8.23.

2,2'-Dinitro-4,4'-bistrifluoromethylsulfonyldisulfide. A solution of sodium disulfide, obtained from 1.2 g of sodium sulfide, 0.16 g of sulfur and 10 ml of alcohol, was added to a solution of 3 g of 4-chloro-3-nitro-phenyltrifluoromethylsulfone in 8 ml of alcohol and the mixture was heated on a water bath. The product was crystallized from glacial acetic acid. The yield was 2.1 g (70%). The m.p. was 223-224°.

Found %: S 22.3, 22.35. $C_{14}H_6O_8N_2S_4F_6$. Calculated %: S 22.37.

2-Methyl-5-trifluoromethylsulfonylbenzothiazole. 2.1 g of the disulfide was dissolved in 12 ml of glacial acetic acid and reduced by the gradual addition of 3.5 g of zinc dust and 9 ml of hydrochloric acid (d 1.19). The solution was diluted with water and sodium acetate was added. The precipitated zinc mercaptide was dried and boiled with 7 ml of acetic anhydride for 3 hours. The product was precipitated with ammonia and crystallized from aqueous alcohol. The yield was 1.2 g (60%). The m.p. was 94-95°.

Found %: N 5.15, 5.25. $C_9H_6NS_2F_3$. Calculated %: N 4.98.

3-Methyl-5-trifluoromethylsulfonylbenzothiazole ethiodide. 0.6 g of 2-methyl-5-trifluoromethylsulfonyl-benzothiazole and 0.4 g of ethyl p-toluenesulfonate were heated for 4 hours in a sealed tube at 140-150°, dissolved in water and the iodide was precipitated by the addition of an aqueous solution of potassium iodide. The yield was 0.6 g (70%).

5,5'-Bis-trifluoromethylsulfonyl-3,3'-diethylthiacarbocyanine iodide. 0.3 g of 2-methyl-5-trifluoromethyl-sulfonylbenzothiazole ethiodide, 0.3 g of orthoformic ester and 2 ml of acetic anhydride were boiled for 45 minutes. The dye was filtered and was crystallized from methyl alcohol. The yield was 0.1 g (38%).

Found %: I 16.59, 16.43. $C_{23}H_{19}O_4N_2S_4F_6I$. Calculated %: I 16.79.

2-p-dimethylaminostyryl-5-trifluoromethylsulfonylbenzothiazole ethiodide. 0.2 g of 2-methyl-5-trifluoro-methylsulfonylbenzothiazole ethiodide, 0.13 g of p-dimethylaminobenzaldehyde and 3 ml of acetic anhydride were boiled for 1 hour. The dye was precipitated with ether. It was crystallized from alcohol. The yield was 0.13 g (50%). The m.p. was 235-236°.

Found %: I 22.13, 22.00. $C_{20}H_{20}O_2N_2S_2F_3I$. Calculated %: I 22.32.

SUMMARY

The synthesis of 4-fluoro-, 4-chloro- and 4-methoxy-3-aminophenyltrifluoromethylsulfones is described. 2-Methyl-6-trifluoromethylsulfonylbenzimidazole, 2-methyl-3-phenyl-6-trifluoromethylsulfonylbenzimidazole and 2-methyl-5-trifluoromethylsulfonylbenzothiazole were obtained. Carbocyanine and the styryl dye were obtained. Carbocyanine and the styryl dye were obtained from the quaternary salt of 2-methyl-5-trifluoromethyl-sulfonylbenzothiazole. It was found that the absorption maximum of thiacarbocyanine with an SO_2CF_3 group in the 5-position of the benzothiazole ring does not differ from the absorption maximum of the unsubstituted dye.

3-Nitro-4-hydrazinophenyltrifluoromethylsulfone was synthesized.

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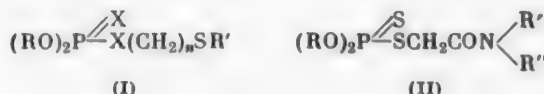[9] H. Zahn and H. Zuber, Ber., 86, 172 (1953).

FROM THE FIELD OF ORGANIC INSECTOFUNGICIDES

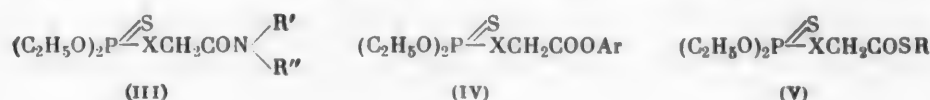## XXXVII. THE SYNTHESIS OF SOME MIXED ESTERS OF THIO- AND DITHIOPHOSPHORIC ACIDS

Ya. A. Mandel'baum, N. N. Mel'nikov and P. G. Zaks

Scientic Institute of Fertilizers and Insectofungicides

In addition to esters of thio- and dithiophosphoric acids with the general formula (I) compounds with the general formula (II) have begun to be used as means of combating undesirable plants [1,2]. The compound known under the conventional name of "acetylurea" may serve as an example of compounds of this type which which have been studied in the USSR [3,4].

$$(RO)_2P \overset{X}{\underset{X(CH_2)_nSR'}{\diagup}} \qquad (RO)_2P \overset{S}{\underset{SCH_2CON}{\diagup}} \overset{R'}{\underset{R''}{\diagdown}}$$

(I) (II)

In connection with the investigation of the relationship between the insecticidal activity of organic compounds of phosphorus and their structure and the search for new contact and systemic insecticides which are not very toxic to warm-blooded animals and man, we carried out a special investigation on the synthesis of mixed esters of thio- and dithiophosphoric acids with the general formulas (III), (IV) and (V).

$$(C_2H_5O)_2P \overset{S}{\underset{XCH_2CON}{\diagup}} \overset{R'}{\underset{R''}{\diagdown}} \qquad (C_2H_5O)_2P \overset{S}{\underset{XCH_2COOAr}{\diagup}} \qquad (C_2H_5O)_2P \overset{S}{\underset{XCH_2COSR}{\diagup}}$$

(III) (IV) (V)

These compounds were synthesized by reacting salts of diethylthiophosphoric and diethyldithiophosphoric acids with the corresponding derivatives of monochloroacetic and monochlorothioacetic acids. The reaction was carried out in acetone with a varying period of heating of the reaction solution. It is interesting to note that, as would be expected on the basis of works [5,6] on the tautomerism of thiophosphoric acid, thionic isomers of thiophosphoric acid were obtained from salts of diethylthiophosphoric acid in all the cases we investigated.

The compounds we synthesized and their properties are given in Table 1. An investigation of the contact insecticidal action on the granary weevil, carried out by V. V. Popov and N. S. Ukrainets, showed that all compounds of this type are inferior to O, O-diethyl-O.4-nitrophenylthiophosphate with respect to their insecticidal activity. It is interesting to note that the most active contact insecticide of this group of substances is O,O-diethyl-O-carbo-4-nitrophenoxymethylphosphate. O,O-diethyl-O-diethylcarbamidomethylthiophosphate is a fairly active systemic acaricide.

EXPERIMENTAL

The preparation of mixed ethers of thio- and dithiophosphoric acids was carried out under the following

conditions: the dry salt of diethylthio-and diethyldithiophosphoric acid and the amide or ester of monochloro-acetic acid (or the ester of monochlorothioacetic acid) were placed in a flask with a reflux condenser and a mechanical stirrer; acetone (120-130 ml of acetone per 0.1 mole of the reacting substances) was added. The reaction mixture was then boiled on a water bath for 5-6 hours. When the reaction had finished the precipitated sodium (or potassium) chloride was filtered, the acetone was distilled and the residue was fractionated under vacuum, after it had been washed with water and dried. Because certain amides with aliphatic amines are fairly readily soluble in water these compounds were not washed with water and after the solvent had been distilled and the residue separated they were fractionated under vacuum. The compounds we obtained and their properties are given in the table.

Properties of Mixed Esters of Thiophosphoric and Dithiophosphoric Acids

Formula	Boiling point (pressure in mm)	Yield (в %)	d_4^{20}	n_D^{20}	P %	
					Found	Calculated
$(C_2H_5O)_2PSOCH_2CON(CH_3)_2$	135—137° (0.4)	64	1.1832	1.4810	12.25	12.15
$(C_2H_5O)_2PSOCH_2CON(C_2H_5)_2$ *	147 (0.35)	70	1.1336	1.4800	10.70	10.85
$(C_2H_5O)_2PSOCH_2CONHC_6H_4NO_2$-2	150—155 (0.3)	53	1.3233	1.5570	9.25	8.90
$(C_2H_5O)_2PSOCH_2CONHC_6H_4NO_2$-3	M.p. 110	62	—	—	8.80	8.90
$(C_2H_5O)_2PSOCH_2CONHC_6H_4NO_2$-4	M.p. 111	75	—	—	8.90	8.90
$(C_2H_5O)_2PSOCH_2COOC_6H_4NO_2$-3	130 (0.3)	52	1.2689	1.5085	8.90	8.99
$(C_2H_5O)_2PSOCH_2COOC_6H_4NO_2$-4	160 (0.5)	48	1.2806	1.5187	8.97	8.89
$(C_2H_5O)_2PSOCH_2COOC_6H_4Cl$-4	125—135 (0.2)	72	1.2787	1.5210	9.10	9.20
$(C_2H_5O)_2PSOCH_2COOC_6H_3Cl_2$-2.4 **	174—177 (0.1)	45	1.3591	1.5310	8.20	8.30
$(C_2H_5O)_2PSOCH_2COSC_2H_5$	133—136 (0.3)	48	1.2041	1.5013	11.05	11.40
$(C_2H_5O)_2PSOCH_2COSC_6H_5$	173—175 (0.2)	70	1.2476	1.5565	9.30	9.70
$(C_2H_5O)_2PSOCH_2COSC_6H_4Cl$-4	150—160 (0.2)	66	1.3141	1.5670	8.50	8.75
$(C_2H_5O)_2PSSCH_2CON(CH_3)_2$	***	59	1.1985	1.5210	11.0	11.40
$(C_2H_5O)_2PSSCH_2CON(C_2H_5)_2$	***	47	1.1478	1.5136	10.30	10.35
$(C_2H_5O)_2PSSCH_2CONHC_6H_4NO_2$-2	***	83	1.2992	1.5950	8.20	8.50
$(C_2H_5O)_2PSSCH_2CONHC_6H_4NO_2$-3	M.p. 102	93	—	—	8.25	8.50
$(C_2H_5O)_2PSSCH_2CONHC_6H_4NO_2$-4	M.p. 112	84	—	—	8.40	8.50
$(C_2H_5O)_2PSSCH_2COOC_6H_4NO_2$-3	M.p. 66—68	45	—	—	8.70	8.49
$(C_2H_5O)_2PSSCH_2COOC_6H_4NO_2$-4	***	48	1.3135	1.5640	8.65	8.49
$(C_2H_5O)_2PSSCH_2COOC_6H_4Cl$-4	170 (0.15)	80	1.2820	1.5540	8.75	8.75
$(C_2H_5O)_2PSSCH_2COSC_2H_5$	140—143 (0.1)	72	1.1961	1.5370	16.65	10.75
$(C_2H_5O)_2PSSCH_2COSC_6H_5$	***	97	1.2321	1.5845	9.50	9.20
$(C_2H_5O)_2PSSCH_2COSC_6H_4Cl$-4	***	98	1.3060	1.5890	8.17	8.40

* Thionic sulfur: found 10.80 %, calculated 11.20%.
** Thionic sulfur: found 8.20%, calculated 8.55%.
*** Not distilled without decomposition at 0.2 mm.

SUMMARY

In order to investigate the relationship between the insecticidal action of mixed esters of thio- and di-thiophosphoric acids and their structure and to find new effective insecticides a number of mixed esters of thio- and dithiophosphoric acids, previously undescribed in literature, were synthesized.

It was shown that the reaction of sodium and potassium diethylthiophosphates with amides and esters of monochloroacetic acid and monochlorothioacetic acid in acetone takes place with the formation of thionic isomers.

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INVESTIGATIONS IN THE FIELD OF DYES FOR ACETATE SILK AND SYNTHETIC FIBERS

II. DISPERSOL DYE, DERIVATIVES OF 1-ALKYLAMINOANTHRAQUINONE-2-CARBOXYLIC ACID [1].

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The acid chloride of 1-nitroanthraquinone-2-carboxylic acid (I) has two reactive groups: the chlorine atom in the acid halide group and the nitro group in the 1-position of the anthraquinone ring, capable of exchange reactions, in particular with amino compounds. In the present instance, the nitro group which, in general is mobile in the anthraquinone ring, is under the positive activating influence of the ortho-located halide group and is very reactive.
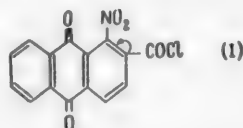
By reacting this acid chloride with aminodiglycol, $H_2NCH_2CH_2OCH_2CH_2OH$, the β-hydroxyethyl- β-hydroxyethylamide of 1-(β'-hydroxyethyl-β-hydroxyethylamino)-anthraquinone-2-carboxylic acid, suitable as a pink dye for acetate silk [2], is formed.

In our investigation of the reactions of the acid chloride of 1-nitroanthraquinone-2-carboxylic acid with other amines the reactivity of the nitro group in some instances was found to be appreciably lower than the activity of the halogen of the acid halide group. The nitro group does not react with diethylamine: when the latter is used the faintly yellow amide of 1-nitroanthraquinone-2-carboxylic acid is formed. When this diethylamide is subsequently treated with primary aliphatic amine the nitro group also reacts with the formation of bluish-red dispersol dyes containing various amine radicals in the 1-position of the anthraquinone ring and in the carboxyl group.

This behavior may be explained by steric hindrance due to the carbonyl group of the anthraquinone ring. It is known that in a number of instances N-disubstituted α-aminoanthraquinones form the far more sterically hindered N-monosubstituted derivatives. In this respect the behavior of piperidine, which readily reacts with both the acid chloride and the nitro group was found to be somewhat different.

The dispersol dyes obtained from the acid chloride of 1-nitroanthraquinone-2-carboxylic acid and aliphatic amines are pink or red dyes for acetate silk, similar to each other as regards tint and other properties. Because of its comparatively high molecular volume, the analogous dye with piperidine does not have an affinity for acetyl cellulose fiber.

EXPERIMENTAL

Methylamide of 1-methylaminoanthraquinone-2-carboxylic acid. 1 g of the acid chloride of 1-nitroanthra quinone-2-carboxylic acid in 20 g of a 20% aqueous solution of methylamine was heated in a hermetically sealed flask to 85°; it was stirred at this temperature for 6 hours, cooled to 20° and the red crystalline substance was filtered; the yield was 0.95 g, the m.p. was 220-221° (from alcohol).

Found %: C 69.10, 69.12; H 4.81, 4.77; N 9.21, 9.28. $C_{17}H_{14}O_3N_2$. Calculated %: C 68.80; H 4.76; N 9.52.

β-Hydroxyethylamide of 1-(β-hydroxyethylamino)-anthraquinone-2-carboxylic acid. 20 g of the acid chloride of 1-nitroanthraquinone-2-carboxylic acid, 20 g of monoethanolamine and 20 g of water were heated to 85° and stirred for 4 hours at this temperature; sodium chloride was added to the cooled solution and the red crystalline substance was filtered; the yield was 27.4 g, the m.p. was 222° (from alcohol).

Found %: N 8.24, 7.74. $C_{19}H_{18}O_5N_2$. Calculated %: N 7.91.

Piperidineamide of 1-piperidinoanthraquinone-2-carboxylic acid. 1 g of the acid chloride of 1-nitro-anthraquinone-2-carboxylic acid, 5 g of piperidine and 15 ml of water were heated and stirred for 6 hours at 85°; when it had cooled the brown crystalline substance was filtered; the yield was 0.85 g, the m.p. was 179-180° (from alcohol).

Found %: N 6.70, 6.76. $C_{25}H_{26}O_3N_2$. Calculated %: N 6.96.

Diethylamide of 1-nitroanthraquinone-2-carboxylic acid. 1 g of the acid chloride of 1-nitroanthraquinone-2-carboxylic acid. 1 g of the acid chloride of 1-nitroanthraquinone-2-carboxylic acid, 5 g of diethylamine and 15 ml of water were heated and stirred for 6 hours at 70°; when it had cooled the almost colorless crystalline substance was filtered; the yield was 0.98 g, the m.p. was 234-235° (from acetic acid and then from isobutyl alcohol).

Found %: C 65.06, 65.24; H 4.43, 4.70; N 8.25, 8.21. $C_{19}H_{16}O_5N_2$. Calculated %: C 64.80; H 4.55; N 7.97.

Diethylamide of 1-methylaminoanthraquinone-2-carboxylic acid. 1 g of the diethylamide of 1-nitro-anthraquinone-2-carboxylic acid, and 10 g of a 20% aqueous solution of methylamine were heated and stirred for 5 hours at 85°, a further 10 g of the 20% methylamine solution was added and the mixture was stirred for another 2 hours at 85°; when it had cooled the red crystalline substance was filtered; the yield was 0.95 g, the m.p. was 112-113° (from aqueous alcohol).

Found %: N 8.44, 8.57. $C_{20}H_{20}O_3N_2$. Calculated %: N 8.33.

Diethylamide of 1-(β-hydroxyethylamino)-anthraquinone-2-carboxylic acid. 1 g of the diethylamide of 1-nitroanthraquinone-2-carboxylic acid, 5 g of monoethanolamine and 15 ml of water were heated and stirred for 6 hours at 85°; when it had cooled the red crystalline substance was filtered; the yield was 0.8 g, the m.p. was 106-107° (from aqueous alcohol).

Found %: N 7.39, 7.33. $C_{21}H_{22}O_4N_2$. Calculated %: N 7.60.

SUMMARY

1. The reactions of the acid chloride of 1-nitroanthraquinone-2-carboxylic acid with certain aliphatic amines and piperidine were investigated.

2. The investigated primary amines and also piperidine react both with the acid chloride group and the nitro group whereas diethylamine reacts only with the acid chloride group. When reacted with primary aliphatic amines, the diethylamine of 1-nitroanthraquinone-2-carboxylic acid formed in the latter instance exchanges its nitro group for a monoalkylamine group.

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COMPARISON OF THE COLOR, REFLECTION AND ABSORPTION
SPECTRA OF ARYLAMIDES OF 3,5-AND 2,4-DINITROBENZOIC ACIDS

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We made a detailed examination of color phenomena associated with arylamides of 2,4-dinitrobenzoic acid and also their reflection and absorption spectra in one of our previous communications [1]. We investigated color phenomena associated with 3,5-dinitrobenzoic acid previous to this [2], but only on the basis of visual observations. The present paper gives the reflection and absorption spectra of 3,5-dinitrobenzoyl derivatives and compares them with the corresponding spectra of derivatives of 2,4-dinitrobenzoyl derivatives. The color of both series of compounds, observed visually, is also compared.

Visual Observations and Reflection Spectra

As may be seen from the data of Table 1 (Expt. No. 2 and 3), in the majority of cases analogous representatives of both of the investigated series of compounds are similar in color. For example, compounds with a p-OCH$_3$ group, examined in powder form, have an orange-yellow color, difficult to distinguish visually (in the crystalline form the 2,4-dinitrobenzoyl derivative has a somewhat deeper color). Compounds with a p-OH group are also close in color. In this connection it is interesting to note that in both series of compounds the derivatives with a p-OH group have a somewhat deeper color than representatives containing a p-OCH$_3$ group (this is particularly noticeable in compounds in the crystalline form) in spite of the fact that, in general, the OH group has more powerful electron-donor properties than the OCH$_3$ group, and compounds with an OH group are generally colored deeper than analogous compounds with an OCH$_3$ group. In the crystalline form, both representatives with p-N(CH$_3$) group are deep red, almost black, the 2,4-dinitrobenzoyl derivative being appreciably darker. In powder form they are red-brown, the 3,5-dinitrobenzoyl derivative having a brighter color. Compounds with a m-N(CH$_3$) group each give forms with two different colors; in this connection both forms of the 3,5-dinitrobenzoyl derivative have a somewhat deeper color than the corresponding forms of the 2,4-dinitrobenzoyl derivative, this being particularly appreciable in the deeper-colored form. Compounds with a m-OH group are very markedly different in color: the 2,4-dinitrobenzoyl derivative is light yellow while the 5,5-dinitrobenzoyl derivative is almost colorless. The almost complete absence of a visible color in the latter compound is somewhat unexpected. In the case of representatives with a m-OCH$_3$ group, the 3,5-dinitrobenzoyl derivative is the most deeply colored.
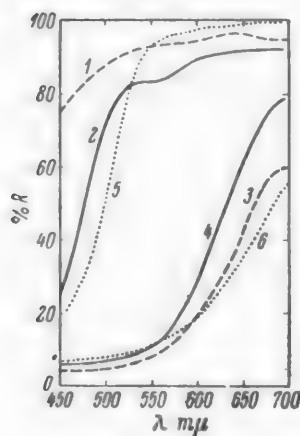
Figs. 1-3 give the reflection-spectra curves of the investigated compounds. From these diagrams it can be seen that with the presence of a m-N(CH$_3$) or m-OCH$_3$ group in the compound the reflection spectra curves of 3,5-dinitrobenzoyl derivatives (Fig. 1, curves 3 and 4; Fig. 2, curves 1 and 2) have a more bathochromic location; on the

Fig. 1. Reflection spectra curves.

1 — 3,5-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$OH-m;
2 — 2,4-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$OH-m;
3 — 3,5-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$N(CH$_3$)$_2$-m;
4 — 2,4-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$N(CH$_3$)$_2$-m;
5 — [3,5-(O$_2$N)$_2$C$_6$H$_3$CONH$_2$ +
   +CH$_3$CONHC$_6$H$_4$OH-m];
6 — [3,5-(O$_2$N)$_2$C$_6$H$_3$CONH$_2$ +
   +CH$_3$CONHC$_6$H$_4$N(CH$_3$)$_2$-m].

TABLE 1

Exp. No.	Types of compounds	Substituting electron-donor groups (A) and color of the corresponding compounds (in powder form)					
		m-OCH$_3$	p-OCH$_3$	m-OH	p-OH	m-N(CH$_3$)$_2$	p-N(CH$_3$)$_2$
1	3-O$_2$NC$_6$H$_4$CONHC$_6$H$_4$A	Colorless	Light-yellow	Pale-yellow	Light-yellow	Yellow-orange	Light-red
2	3,5-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$A	Pale-yellowish	Orange-yellow	Almost colorless	Bright-yellow	Brownish-red •	Reddish-brown
3	2,4-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$A	Almost colorless	Orange-yellow	Yellow	Yellow	Brownish-red •	Reddish-brown
4	4-O$_2$NC$_6$H$_4$CONHC$_6$H$_4$A	Slightly yellow	Slightly yellow	Light-yellow	Orange-yellow	Pale-brown	Light-red

•The second form of this compound is orange-red (in powder form). Both forms of the 3,5-dinitrobenzoyl derivative have a somewhat deeper color than the corresponding forms of the derivative of the 2,4-dinitrobenzoyl derivative.

other hand, with the presence of a m-OH group the curve of 2,4-dinitrobenzoic acid (Fig. 1, curves 1 and 2) has a more bathochromic location . This corresponds to the relative depth of color of the indicated compounds, observed visually. In the case of compounds containing an electron-donor group in the para-position, the curves of the 3,5-dinitrobenzoyl derivatives in all instances intersected the curves of the corresponding 2,4-dinitrobenzoyl derivatives; at times this makes it difficult to decide which of the compounds has the deepest color. In general, the upper "horizontal" part of the curve is located higher in the former than in the latter. This evidently matches the brighter color of the 3,5-dinitrobenzoyl derivatives. As regards the ascending branch of the curve, the relative position of which mainly determines the depth of color of the corresponding compounds, the following picture is found: in compounds with a p-OH group a considerable part of the ascending branch of the curve (up to the point of intersection) has a more bathochromic location in the 3,5-dinitrobenzyol derivatives which also has a somewhat deeper color when visually observed (Fig. 3, curves 1 and 2). In the case of representatives with a p-N(CH$_3$) group, on the other hand, a considerable part of the ascending branch of the curve (above the point of intersection) has a more bathochromic location in the 2,4-dinitrobenzoyl derivative and only the lower smaller part of the curve has a more bathochromic location in the 3,5-dinitrobenzoyl derivative (Fig. 3, curves 3 and 4). In this case the 2,4-dinitrobenzoyl derivative has a deeper color. The relative location of the reflection curves in the case of compounds with a p-OCH$_3$ group suggests a some-what different picture to that just considered: in this case a considerable part of the ascending branch of the curve also has a more bathochromic location in the 2,4-dinitrobenzoyl derivative (Fig. 2, curves 3 and 4); this evidently also agrees with the fact that this compound has a deeper color than the analogous 3,5-dinitrobenzoyl derivative (when the compounds are examined in powder form this difference is difficult to detect by visual means).

Absorption Spectra

Figs. 4-6 give the absorption-spectra curves of 3,5-dinitrobenzoyl derivatives and the corresponding curves of the 2,4-dinitrobenzoyl derivatives. Both sets of curves have a clearly expressed short-wave maximum which in the case of the 3,5-dinitrobenzoyl derivatives generally has a greater intensity and is displaced in the direction of the shorter waves compared with the maximum of the corresponding 2,4-dinitrobenzoyl derivatives. In the case of the 3,5-dinitrobenzoyl derivatives the long-wave band, which enters the visible part of the spectrum, also has a somewhat greater absorption intensity in all instances but is narrower than in the 2,4-dinitrobenzoyl derivatives; in the 3,5-dinitrobenzoyl derivatives the lower ascending branch of the curve, which characterizes the absorption of
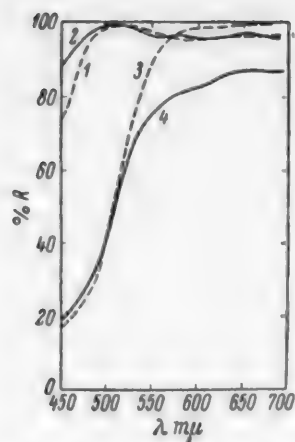
Fig. 2. Reflection-spectra curves.

1) 3,5-(O₂N)₂C₆H₃CONHC₆H₄OCH₃-m;
2) 2,4-(O₂N)₂C₆H₃CONHC₆H₄OCH₃-m;
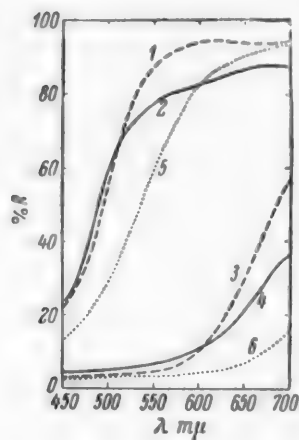3) 3,5-(O₂N)₂C₆H₃CONHC₆H₄OCH₃-p;
4) 2,4-(O₂N)₂C₆H₃CONHC₆H₄OCH₃-p.

Fig. 3. Reflection-spectra curves

1 — 3,5-(O₂N)₂C₆H₃CONHC₆H₄OH-p;
2 — 2,4-(O₂N)₂C₆H₃CONHC₆H₄OH-p;
3 — 3,5-(O₂N)₂C₆H₃CONHC₆H₄N(CH₃)₂-p;
4 — 2,4-(O₂N)₂C₆H₃CONHC₆H₄N(CH₃)₂-p;
5 — [3,5-(O₂N)₂C₆H₃CONH₂ +
  CH₃CONHC₆H₄OH-p
6 — [3,5-(O₂N)₂C₆H₃CONH₂ +
  +CH₃CONHC₆H₄N(CH₃)₂-p].

light in the visible part of the spectrum, is, therefore, always located more hypsochromically than in the 2,4-dinitrobenzoyl derivatives. Judging the relative depth of color of the investigated compounds from the position of the ascending branch of the curve, characterizing the absorption of visible light, it is, therefore, found that in solution all representatives of the 3,5-dinitrobenzoyl series are always less deep in color than the isomeric compounds of the 2,4-dinitrobenzoyl series. As already mentioned above, in the case of substances in the solid state no such regularity is observed and the 3,5-dinitrobenzoyl derivatives are sometimes more deeply colored than the corresponding representatives of the 2,4-dinitrobenzoyl series. This difference in the relative depth of color between substances in solid form and in solution may be considered as a proof that in the investigated compounds equimolecular forces take part in the reaction between the electrophilic and electron-donor systems, which is the main factor determining their color [3].

The possibility of an exomolecular reaction between electrophilic and electron-donor systems in the case of the dinitrobenzoyl derivatives is also indicated by the following fact: in the solid form the complexes we obtained from 3,5-dinitrobenzamide and acetylated amines, containing an additional electron-donor group (A) [CH₃CONHC₆H₄A, where A = OCH₃, OH, N(CH₃)₂], i.e. from compound having electrophilic and electron-donor systems analogous to such dinitrobenzoyl derivatives, have a color which is fairly similar to that of the latter [2]. In addition to the reflection-spectra curves of 3,5-dinitrobenzoyl derivatives Figs. 1-3 give the reflection-spectra curves of their corresponding complex compounds. In general, the latter have a more bathochromic location than the former.

As regards the maximum of the long-wave absorption band, in both the series of investigated compounds it is indistinctly expressed and in nearly all cases its position can only be determined approximately: at 320-325 mμ in compounds containing an OH or OCH₃ group in the para-position and at 300 mμ in compounds containing the same groups in the meta-position. In compounds with a m-N-CH₃)₂ group this maximum is expressed very indistinctly; on the other hand, in compounds containing the same group in the para-position it is shown most clearly, particularly in the case of the 2,4-dinitrobenzoyl derivative, where its position can be determined with complete accuracy (400 mμ).

In addition to the two above-mentioned absorption bands all the curves of compounds containing an electron-donor group (A) in the meta-position also have a small projection located between them. In the 3,5-dinitrobenzoyl derivatives this projection is much less pronounced than in the 2,4-dinitrobenzoyl derivatives. It is most clearly expressed in compounds with a m-N(CH₃)₂ group.

It is interesting to note that there is a clearly expressed maximum (306 mμ) in this region in the curve of a 3,5-dinitrobenzoyl derivative containing a N(CH₃)₂ group, in the para-position.

A comparison of the absorption curves of 3,5-dinitrobenzoyl derivatives with the composite curves, plotted on the basis of the sum of the absorption of two individual components, one of which contains an analogous electrophilic group [3,5-(O₂N)₂C₆H₃CONH₂], and the other an analogous electron-donor system(CH₃CONHC₆H₄A) shows that, as in the case of the 2,4-dinitrobenzoyl derivatives, both curves are considerably different from each
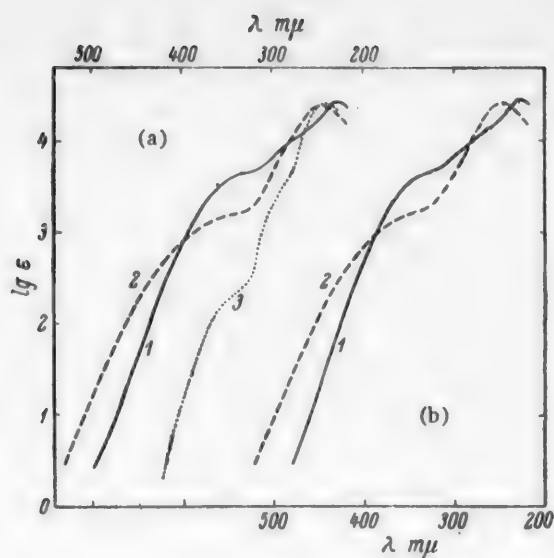
Fig. 4. Absorption-spectra curves.

(a) 1) 3,5-(O₂N)₂C₆H₃CONHC₆H₄OH-p; 2)
2,4-(O₂N)₂C₆H₃CONHC₆H₄OH-p; 3) curve of the sum of the absorp-
tions : 3,5-(O₂N)₂C₆H₃CONH₂+CH₃CONHC₆H₄OH-p; (b) 1)
3,5-(O₂N)₂C₆H₃CONHC₆H₄OCH₃-p, 2)
2,4-(O₂N)₂C₆H₃CONHC₆H₄OCH₃-p.

other (Figs. 4-6). In both series of compounds this difference is shown primarily in a broadening of the long-wave band as a result of which the absorption boundaries in the visible part of the spectrum are strongly displaced towards the longer waves; the absorption intensity increases simultaneously. In general, the values of the displacements of the absorption boundary are always somewhat less for the 3,5-dinitrobenzoyl derivatives than for the corresponding 2,4-dinitrobenzoyl derivatives; for analogous compounds of both series they are always greater when an electron-donor group, located in the para-position, is present, particularly in the case of compounds with a p-N(CH₃)₂ group.

The appreciable difference of the absorption spectra curves of both the 2,4- and 3,5-dinitrobenzoyl derivatives from their corresponding composite curves leads to the conclusion that in both series of compounds the reaction between the electrophilic and electron-donor systems can be effected intramolecularly, along a chain, as well as intermolecularly. The former is possible owing to the fact that the CONH group is capable of tautomerism [1], which causes the appearance in the compound of a continuous conjugated chain of double bonds, serving as a conductor of electron displacements (I and II).
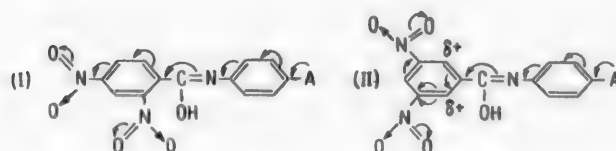
In the case of 2,4-dinitrobenzoyl derivatives containing an electron-donor group in the para-position, groups of opposing character — electrophilic (NO₂) and electron-donor (A) are found to be located at the ends of the conjugated chain formed in this way. This results in the possibility of electron displacement along the whole length of the chain, from the electron-donor group to the electrophilic group (I). In the case of the 3,5-dinitrobenzoyl derivatives none of the nitro groups forms the end of the conjugated chain and these groups can, therefore, only exert an inductive influence on the electron displacements along the chain (caused by the presence of a para-electron-donor group); this influence is due to the appearance of a positive charge on the carbon atoms located in the ortho position with respect to the CO group (II). As a result the curves of the 3,5-dinitrobenzoyl derivatives with an electron-donor group in the para-position are always more hypsochromically located than the curves of the corresponding 2,4-dinitrobenzoyl derivatives.

Both in the 2,4- and 3,5-dinitrobenzoyl series of derivatives, when a meta-located electron-donor group is present, this group does not form the end of a conjugated chain and can only exert an inductive influence on the electron displacements taking place in the latter, owing to the appearance of a negative charge on the carbon atom located in the ortho-position with respect to the NH-group. The absorption curves of the corresponding compounds are, therefore, always located more hypsochromically than the curves of the isomers containing the same groups in the para-position. The possibility of the direct influence of the nitro-groups (field effect) on the electron displacements taking place in the chain must also be taken into consideration. The latter can appear in both the 2,4- and 3,5-dinitrobenzoyl derivatives regardless of the position in which the additional electron-donor group is located.
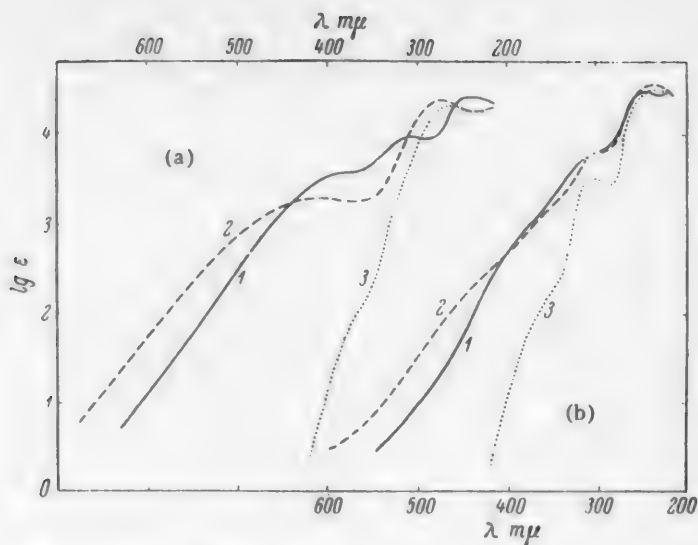
Fig. 5. Absorption-spectra curves.

(a) 1) 3,5-(O₂N)₂C₆H₃CONHC₆H₄N(CH₃)₂-p;
2) 2,4-(O₂N)₂C₆H₃CONHC₆H₄N(CH₃)₂-p; 3) curve of the sum of the absorptions: 3,5-(O₂N)₂C₆H₃CONH₂+CH₃CONHC₆H₄N(CH₃)₂-p;
(b) 1) 3,5-(O₂N)₂C₆H₃CONHC₆H₄N(CH₃)₂-m;
2) 2,4-(O₂N)₂C₆H₃CONHC₆H₄N(CH₃)₂-m;
3) curve of the sum of the absorptions: 3,5-(O₂N)₂C₆H₃CONH₂+
+CH₃CONHC₆H₄N(CH₃)₂-m.
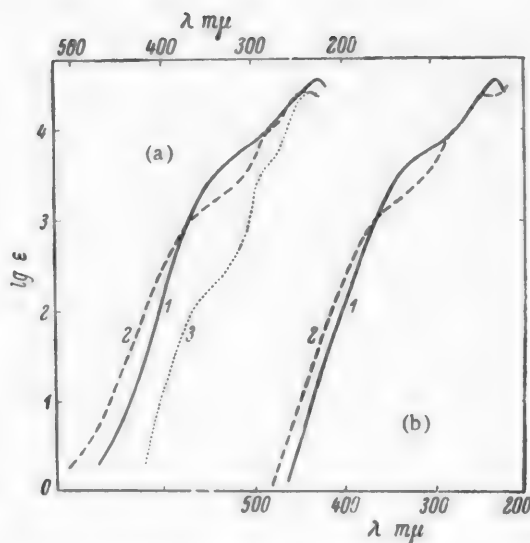
Fig. 6. Absorption-spectra curves.

(a) 1) 3,5-(O₂N)₂C₆H₃CONHC₆H₄OH-m
2) 2,4-(O₂N)₂C₆H₃CONHC₆H₄OH-m 3) curve
of the sum of the absorptions : 3,5-(O₂N)₂C₆H₃CONH₂+
+CH₃CONHC₆H₄OH- m;
(b) 1) 3,5-(O₂N)₂C₆H₃CONHC₆H₄OCH₃-m;
2) 2,4-(O₂N)₂C₆H₃CONHC₆H₄OCH₃-m.

The Influence of the Introduction of a Second Nitro Group in Aryl Amides of 3-Nitrobenzoic and 4-Nitrobenzoic Acids On the Color of the Substance

As we have previously established [1], in the majority of cases the introduction of a second NO₂ group in the molecule of a 4-nitrobenzoyl derivative (in the 2-position) leads to a deepening in the color of the compound and a bathochromic displacement of the reflection-spectrum curve, the effect being greatest when a p-N(CH₃)₂ group is present in the compound; sometimes, however, when, for example, a p-OH or m-OCH₃ group is present in the compound, the opposite effect is also observed, i.e. the introduction of a second nitro group causes an increase in the color and the reflection spectrum curve is displaced hypsochromically. In all cases, however, the absorption spectrum curves undergo a bathochromic displacement as a result of this introduction. In solution, all the 2,4-dinitro-benzoyl derivatives therefore have a deeper color than the corresponding 4-mononitro compounds, in contrast to their appearance in the solid state.

In almost all cases the introduction of a second nitro group in the molecule of the 3-nitrobenzoyl derivative (in the 5-position) is accompanied by a deepening in the color of the compounds (Table 1)

and the bathochromic displacement of the reflection-spectrum curves (Figs. 7, 8, 9) and absorption spectrum curves (Table 2.). A compound with a m-OH group forms the sole exception; with the presence of two nitro groups in it a compound of this type is found to be less deeply colored than the corresponding mononitro compound and the reflection-spectrum curve corresponding to it is displaced hypsochromically with respect to the reflection-spectrum curve of the mononitro derivative (Fig. 7). We believe that as in the case of the 2,4-dinitrobenzoyl derivatives, the cause of this must be sought in the complexity of the reaction conditions of the electrophilic and electron-donor systems, the reaction taking place both intramolecularly along the chain and also by means of exomolecular forces. The latter can only be developed to the full extent, however, in a substance in the solid state; in solutions, particularly in the very dilute ones used in spectral analysis, the exomolecular reaction is either considerably or completely disturbed. To illustrate this point (with reference to the case in question) Fig. 10 shows the absorption-spectrum curves of the complex formed by 3,5-dinitrobenzamide and 4-acetaminodimethylaniline, i.e. compounds having the same electrophilic and electron-donor systems as the corresponding 3,5-dinitrobenzoyl derivative. These curves were determined at comparatively high concentrations (10^{-2} and $3 \cdot 10^{-2}$ mole). Fig. 10 gives both the curves corresponding to the individual components of the complex and the composite curve obtained on the basis of the sum of the absorptions of these components. From the curves given it can be seen that even with a comparatively high solution concentration ($3 \cdot 10^{-2}$ mole) the absorption of light in the visible part of the spectrum corresponding to the complex (lower "horizontal" branch of the curve) is very slight. As a result of the dilution of the solution with three parts of water this absorption is still further reduced and in the case of extremely dilute solutions (10^{-3} and 10^{-4} mole) it must naturally be completely absent.
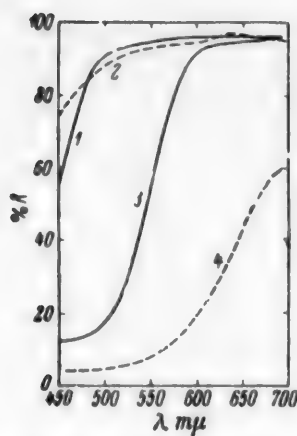
Finally, the following fact must be taken into consideration: the exomolecular reaction can sometimes be disturbed in the substance in the solid state also, this process generally leading to the formation of a colorless form. We were obliged to deal with facts of this type on a previous occasion [4]. It is possible that in the case in question, i.e. with compounds containing an OH group in the meta-position, we are dealing with a similar type of phenomenon. The slight visible color of this compound is due to the possibility of the reaction of chromophoric systems along the chain, which in the presence of either a nitro or OH group in the meta-position is naturally accompanied by only a very insignificant optical effect.

Table 2 gives the values of the displacements of the reflection and absorption-spectrum curves and the short-wave maximum of light absorption, observed as a result of the introduction of a second NO_2 group in the 3-nitro and 4-nitrobenzoyl derivatives in the 5 and 2 positions, respectively. From the data of this table it can be seen that for substances in the solid form (reflection-spectrum curves) a more powerful effect from the introduction of a second NO_2 group is observed in some cases in the first series of compounds while in others it occurs in the second, the maximum values being attained in compounds containing the most powerful electron-donor group $N(CH_3)_2$. This effect is sometimes negative (hypsochromic), also. For substances in the dissolved state the displacement of the absorption curves, observed as a result of the conversion of the mononitro compounds to the corresponding dinitro derivatives, is always positive (bathochromic) being nearly

Fig. 7. Reflection-spectrum curves.

1 — 3-O$_2$NC$_6$H$_4$CONHC$_6$H$_4$OH-m;
2 — 3,5-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$OH-m.
3 — 3-O$_2$NC$_6$H$_4$CONHC$_6$H$_4$N(CH$_3$)$_2$-m,
4 — 3,5-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$N(CH$_3$)$_2$-m.

Fig. 8. Reflection-spectrum curves.

1 — 3-O$_2$NC$_6$H$_4$CONHC$_6$H$_4$OCH$_3$-m;
2 — 3,5-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$OCH$_3$-m;
3 — 3-O$_2$NC$_6$H$_4$CONHC$_6$H$_4$OCH$_3$-p;
4 — 3,5-(O$_2$N)$_2$C$_6$H$_3$CONHC$_6$H$_4$OCH$_3$-p.

always greater in the series of 3,5-dinitrobenzoyl derivatives On the other hand, in both series of compounds the short-wave maximum is nearly always displaced hypsochromically.

Spectral Measurements

We measured the absorption spectra in a Beckmann spectrophotometer. Alcohol (rectified) and acetone were used as the solvent. Both solvents were distilled in a column, the acetone being distilled after first drying over potash. The more dilute solution (10^{-5} and 10^{-4} mole) were prepared in alcohol, the more concentrated ones (0.5 10^{-3} mole) in acetone.

The reflection spectra were measured in the apparatus described by E. V. Shpol'skii [5]. The details of the measurements were given by us previously [6].
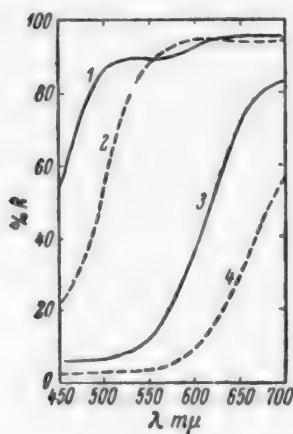

Fig. 9. Reflection spectrum curves.

1) $3\text{-}O_2NC_6H_4CONHC_6H_4OH\text{-}p$;
2) $3,5\text{-}(O_2N)_2C_6H_3CONHC_6H_4OH\text{-}p$;
3) $3\text{-}O_2NC_6H_4CONHC_6H_4N(CH_3)_2\text{-}p$;
4) $3,5\text{-}(O_2N)_2C_6H_3CONHC_6H_4N(CH_3)_2\text{-}$ p.
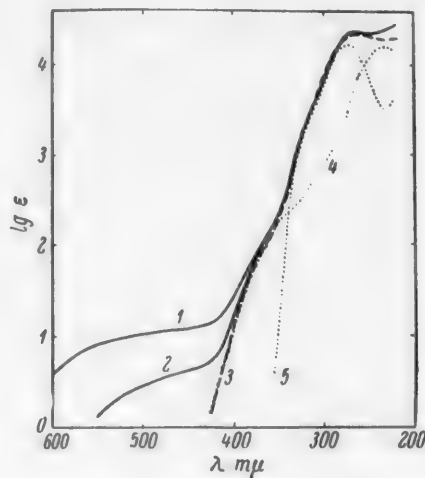
Fig. 10. Reflection spectrum curves.

1) $[3,5\text{-}(O_2N)_2C_6H_3CONH_2 +$ $+CH_3CONHC_6H_4N(CH_3)_2\text{-}p]$, $3 \cdot 10^{-3}$ м.;
2) $[3,5\text{-}(O_2N)_2C_6H_3CONH_2 +$ $+CH_3CONHC_6H_4N(CH_3)_2\text{-}p]$, 10^{-3} м.;
3) curve of the sum of the absorptions 4 and 5;
4) $3,5\text{-}(O_2N)_2C_6H_3CONH_2$;
5) $CH_3CONHC_6H_4N(CH_3)_2\text{-}p$.

TABLE 2

Displacement (in $m\mu$) of the Reflection and Absorption Spectrum Curves in the Short-Wave Absorption Maximum as a Result of the Introduction of a Second Nitro Group in Aryl Amides of 3-Nitrobenzoic and 4-Nitrobenzoic Acids*

Electron donor group (A)	Displacement of the reflection-spectrum curves			Displacement of the absorption-spectrum curves with lgε = 1		Displacement of the short-wave maximum	
	3.5**	2.4**	%R	3.5-	2.4-	3.5-	2.4-
$p\text{-}N(CH_3)_2$	+ 60	+ 80	20	+ 108	+ 46	−10	−14
$m\text{-}N(CH_3)_2$	+ 96	+ 50	20	+ 34	+ 43	− 8	0
$p\text{-}OH$	+ 50	− 35	60	+ 52	+ 17	−37	− 4
$m\text{-}OH$	− 10	+ 46	80	+ 12	+ 7	−36	− 7
$p\text{-}OCH_3$	+ 54	+ 58	60	+ 36	+ 21	−40	− 3
$m\text{-}OCH_3$	+ 20	+ 20	90		+ 13		− 6

*Plus sign = bathochromic displacement, minus sign = hypsochromic displacement,

**The figures signify the position of the nitro groups in the dinitro derivatives formed.

SUMMARY

1. A comparison of the color of aryl amides of 3,5-dinitrobenzoic acid, with the general formula 3,5-$(O_2N)_2C_6H_3CONHC_6H_4A$, with the color of the corresponding aryl amides of 2,4-dinitrobenzoic acid shows that in some cases (A = m-OCH_3, p-OH, m-$N(CH_3)_2$) the former have a deeper color while in other cases (A = m-OH, p-$N(CH_3)_2$, p-OCH_3) this is true of the latter.

2. The reflection spectra, measured for substances in the solid state, confirm the visual observations and increase their accuracy.

3. A comparison of the absorption spectra of both series of compounds shows that in solution all the representatives of the 3,5-dinitrobenzoyl series are less deeply colored than the corresponding representatives of the 2,4-dinitrobenzoyl series.

4. This difference in the relative depth of color of the substances in the solid state and in solution may be considered as proof that exomolecular forces take part in the reaction between the electrophilic and electron-donor systems, this reaction being the main factor governing the color of the investigated compounds. These forces can only appear to the full extent in substances in the solid form, whereas in dilute solutions, they are disturbed to a considerable extent.

5. The similarity between the color of the 3,5-dinitrobenzoyl derivatives and that of the complexes obtained from components containing the same electrophilic [3,5-$(O_2N)_2C_6H_3CONH_2$] and electron-donor [($CH_3CONHC_6H_4A$] systems as the dinitro derivatives is confirmation of the possibility of a similar intermolecular reaction in the case of the dinitrobenzoyl derivatives, also.

6. The marked difference in the absorption curves of aryl amides of 3,5-dinitrobenzoic acid (as in the case of arylamides of 2,4-dinitrobenzoic acid) and the curves plotted on the basis of the sum of the absorptions of the above-mentioned individual components may be considered as proof that in the 3,5-dinitro derivatives the reaction between the electrophilic and electron-donor systems also takes place intramolecularly along a chain of double bonds. The latter is formed as a result of the tautomerism of the CONH group to the -C=N- group.
    OH

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INVESTIGATION IN THE FIELD OF ORGANIC ISOCYANATES

V . THE MECHANISM OF CONVERSIONS OF ARYL ISOCYANATES UNDER THE
INFLUENCE OF ALUMINUM CHLORIDE

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In previous communications it was shown that with fused $AlCl_3 \cdot NaCl$,phenyl isocyanate and its cyclic dimer give 3-phenyl-2,4-dioxotetrahydroquinazoline [1] and naphthyl isocyanate is converted into naphthostyryl [2]. Aryl isothiocyanates form the corresponding thionic compounds [3]. The purpose of the present paper is to discuss the mechanism of these conversions.

Two molecules of phenyl isocyanate (I)take part in the formation of(V)3-phenyl-2,4-dioxotetrahydroquinazoline, making it possible to assume the preliminary dimerization of the isocyanate. The cyclic dimer (IV), the structure of which was recently convincingly proven by x-ray data [4], is only formed from the monomer by the action of tertiary amines or phosphines. At low temperature aluminum chloride converts phenyl isocyanate to the cyclic trimer, triphenyl isocyanurate (VI). Under these conditions the dimer of phenyl isocyanate remains unchanged and with fused $AlCl_3 \cdot NaCl$ gives a derivative of quinazoline (V) [1], whereas the trimer is stable when acted on by $AlCl_3$ at increased temperature. The formation of (V) from phenyl isocyanate is observed not only in a dilute mixture of the salts but also as a result of the action of $AlCl_3$ in organic solvents at 130-160°. In consequence, the only factor determining the formation of different products from phenyl isocyanate is the temperature.

Polymerization of the isocyanate must precede the formation of active forms capable of reacting together. All known facts regarding reactions with aluminum chloride exclude the assumption of an intermediate compound with a biradical character. The assumption of the formation of addition products at the multiple bonds meets a number of strong objections. As was shown by the experiments, the addition product of the elements of hydrogen chloride, the acyl chloride of phenylchlorocarbamic acid, does not give a quinazoline derivative with $AlCl_3 \cdot$ NaCl. In addition, with a negligible HCl content in the reaction mass it is difficult to explain the comparatively high rate of the conversions observed in this case. What has been said above also relates to the possibility of the addition of members of the $HAlCl_4$ molecule. In the case of the addition of members of the molecules of Al_2Cl_6 or $NaAlCl_4$ (for the mixture of salts) at the multiple bonds the bond of the members of these molecules with the organic molecule must , to a considerable extent, be polar and the effect will obviously correspond to the polarization of the isocyanate molecule (II). The polarization hypothesis remains the most probable and agrees well with the formation of trimers from aryl isocyanates under the influence of carbonates, acetates, formates, phenoxydes, alkoxides of the alkali and alkaline earth metals, oxalic acid and other similar substances [5]. It is interesting to note that $AlCl_3$ and the above-mentioned substances also increase the rate of reaction of isocyanates with compounds containing active hydrogen [5].

It is probable that the reaction product of two polarized molecules of phenyl isocyanate (III) is common for the formation of both (VI) and (V). At low temperature, with the participation of a third polarized isocyanate molecule,a trimer is obtained. At increased temperature the activation of the aromatic ring and the kinetic advantages of intramolecular cyclization determine the direction of the reaction in favor of (V). The cyclic dimer (IV) is not the intermediate but the initial product of the synthesis of (V). The four-membered ring is

ruptured comparatively easily by the action of aluminum chloride. With benzene and AlCl₃ the dimer of phenyl isocyanate gives benzanilide, possibly as a result of the reaction of the initially formed N-benzoyl-N,N'-diphenyl-urea with a fresh molecule of benzene. It is known that with ammonia and alcohol the dimer of phenyl iso-cyanate gives derivatives of biuret [6] and allophanic acid [7], with phenol it gives phenylcarbamic ester [6]. The conversions of phenyl isocyanate and its cyclic dimer under the influence of AlCl₃ is shown in the system.
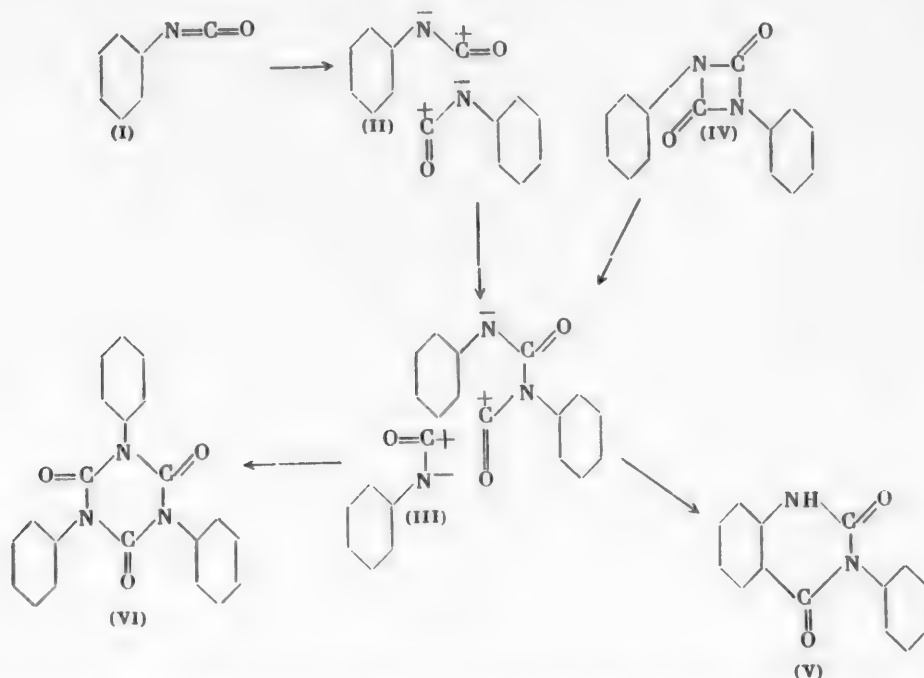
The reaction of aluminum chloride with the carbonyl group and the aromatic ring is not the issue here; in this respect the investigated processes do not differ from ordinary Friedel-Crafts acylation. In the case of 1-naphthyl isocyanate, other geometrical relationships determine the possibility of cyclization within one polarized molecule.
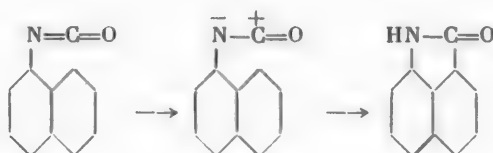
According to Leuckart [8] the reaction with benzene in the presence of AlCl₃ precedes the addition of the elements of HCl to the phenyl isocyanate molecule with the formation of the acyl chloride of phenylcarbamic acid. From kinetic considerations this suggestion has little probability. As a result of the low HCl content in the mass, when the course of the reaction is of this type the main reaction product must be triphenyl iso-cyanurate, not benzanilide. Instead, it is more probable to see complete analogy with the formation of cyclic products from aryl isocyanates. The high activity of the hydrogen atom in benzene determines substitution in the aromatic ring at a lower temperature. Together with 3-phenyl-2,4-dioxotetrahydroquinazoline, small quantities (about 10%) of a product insoluble in aqueous alkali are formed from phenyl isocyanate in fused AlCl₃ · NaCl. In its elementary composition this colorless infusible amorphous substance is similar to phenyl isocyanate. 4-Aminobenzoic acid was found in its decomposition products after heating with alcoholic alkali. The substitution of hydrogen in the para-position to the isocyanate group is, therefore, also represented to a

small extent; this leads to a compound which, judging from its analysis and physical constants, is formed from the radicals of a large number of molecules of 4-aminobenzoic acid, probably connected in a chain.

EXPERIMENTAL

0.9 g of AlCl₃ was added with stirring to 1.79 g of phenyl isocyanate. The mass rapidly solidified. It was mixed with 20 ml of absolute methanol and 10 ml was distilled off; it was then diluted with 200 ml of dry benzene and filtered. The filtrate was evaporated to 15 ml and cooled. The crystalline precipitate was filtered and crystallized from ethyl alcohol . The weight was 1.3 g. It was in the form of prisms. The m p. was 280.1–282.0°. A mixture with triphenyl isocyanurate, obtained by a known method (m.p. 278.5-280.4°), melted at 278.6-281.4°.

23.8 g of phenyl isocyanate was introduced over a period of 20 minutes at 130-135° into a mixture of 135 g of AlCl₃ and 32 g of NaCl; it was stirred for 30 minutes and poured into a mixture of water and ice, acidified with HCl. The precipitate was filtered, washed with dilute hydrochloric acid and water. 0.69 g (3.7%) of aniline, identified in the form of an azo dye with 2-naphthol, was found in the filtrate by titrating with 0.5 N NaOH. After it had been dried the precipitate (21.1 g, 88.5% of the weight of phenyl isocyanate taken) was mixed with 500 ml of 5% aqueous KOH; it was then filtered and washed with water on the filter. 17.85 g (75%) of 3-phenyl-2,4-dioxotetrahydroquinazoline was precipitated from the filtrate by hydrochloric acid. It was in the form of lancet-like crystals from CH₃COOH. The m.p. was 280.0-281.4°. The alkali-insoluble residue was 2.7 g, 11.3% of the weight of phenyl isocyanate used. It was an amorphous, almost colorless product, insoluble in aqueous alkalis and acids, very difficultly soluble in organic substances. It was purified by extraction with boiling glacial CH₃COOH.

Found %: C 71.17. 71.10; H 4.70, 4.73; N 10.93, 11.03.

The purified product was boiled with 20% alcoholic KOH for 8 hours. 4-Aminobenzoic acid, identified in the form of the azo dye with 2-naphthol, was found in the solution. The m.p. was 292.0-294.0°. A mixture with the dye, obtained from 2-naphthol and 4-aminobenzoic acid (m.p. 292.5-294°), melted at 292.5-294°.

6.0 g of phenyl isocyanate in 30 ml of o-dichlorobenzene was added over a period of 10 minutes to 16 g of AlCl₃ in 90 ml of o-dichlorobenzene, heated to 160°. It was stirred for 2 hours and poured into 800 g of ice and 50 ml of conc. HCl. The dichlorobenzene was steam distilled, the residue was filtered and washed with water. The precipitate was mixed with 300 ml of 5% aqueous KOH and 3-phenyl-2,4-dioxotetrahydroquinazoline was precipitated from the filtrate with hydrochloric acid. The yield was 1.76 g (29%). A solution of isocyanate, obtained by the action of phosgene on aniline in dichlorobenzene or trichlorobenzene, could be used for the reaction.

3.0 g of the dimer of phenyl isocyanate (m.p. 175.0-176.0°) was introduced into 20 ml of carbon bisulfide, and 1.7 g of AlCl₃ was added. The mixture was stirred for 7 hours at 25°, filtered and washed with carbon bisulfide. The precipitate was boiled with 50 ml of ethyl alcohol and filtered. The dimer of phenyl isocyanate, with a m.p. of 176.8-177.4°, was precipitated from the filtrate on cooling. A mixture with the initial product melted at 176.6-177.2°. After the evaporation of the carbon bisulfide, the dimer of phenyl isocyanate, with a m p. of 174.0-175.0°, was also obtained.

3.36 g of AlCl₃ was added to 2.0 g of the dimer of phenyl isocyanate in 30 ml of benzene and stirred for 3 hours at 60°. The mixture was poured on to ice and the benzene was distilled off; it was then filtered, and washed and dried. 4.93 g of a substance with an m.p. of 155-157° was obtained. After crystallization from ethyl alcohol the m.p. was 161.2-163.2°. It was identified with benzanilide obtained from aniline and benzoyl chloride.

10.0 g of triphenyl isocyanate with an m.p. of 278.5-280.4° was added to a fused mixture of 80 g of AlCl₃ and 20 g of NaCl and stirred for 30 minutes at 136-140°. It was poured on to ice, filtered, washed and dried. The weight was 9.8 g. After crystallization from alcohol 7.2 g of a substance with an m.p. of 275.3-278.0° was obtained. A mixture with the initial product melted at 275.7-279.4°.

10.0 g of the acyl chloride of phenylcarbamic acid (obtained by the action of dry HCl on phenyl isocyanate in chloroform) was added at 130-135° to a fused mixture of 80 g of AlCl$_3$ and 20 g of NaCl; the mixture was stirred for 30 minutes, poured on to ice, filtered and washed. The pale-violet precipitate (3.5 g) was found to be impure diphenylurea. 2.3 g of aniline, identified in the form of the azo dye with 2-naphthol, was found in the filtrate by titration with 0.5 N NaNO$_2$.

SUMMARY

1. Under the influence of AlCl$_3$, phenyl isocyanate forms a trimer, triphenyl isocyanate, and at increased temperature, 3-phenyl-2,4-dioxotetrahydroquinazoline.

2. At low temperature the dimer of phenyl isocyanate, 1,3-diphenylurethidine-2,4-dione, is stable when acted on by AlCl$_3$. At increased temperature it is converted to 3-phenyl-2,4-dioxotetrahydroquinazoline; with benzene and AlCl$_3$ the dimer forms benzanilide.

3. Triphenyl isocyanate resists the action of fused AlCl$_3$ · NaCl.

4. When acted on by AlCl$_3$ the acyl chloride of phenylcarbamic acid does not form 3-phenyl-2,4-dioxo-tetrahydroquinazoline.

5. The conversion of aryl isocyanates under the influence of AlCl$_3$ is associated with the partial polarization of the multiple nitrogen-carbon bond and, at increased temperature, with the activation of the aromatic ring.

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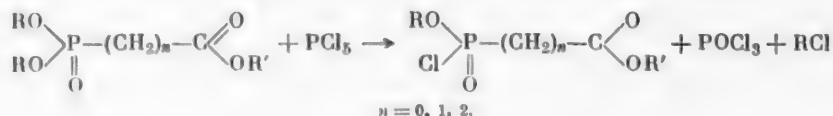[7] W. Frentzel, Ber., 21, 411 (1888).

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ACYL HALIDES OF ESTERS OF PHOSPHONOALKANE CARBOXYLIC ACIDS •

1. THE SYNTHESIS OF P-MONOACYL CHLORIDES OF DIALKYL ESTERS OF PHOSPHONOALKANE CARBOXYLIC ACIDS

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The acyl halides of phosphonoalkane carboxylic acids are unsaturated substances. Only one representative of this type of compound, the triacyl chloride of phosphonoacetic acid [1,2], is known. The present paper is devoted to an investigation of methods of obtaining P-acyl chlorides of dialkyl esters of phosphonoalkane carboxylic acids, which were obtained mainly by the action of phosphorus pentachloride on medium esters of phosphonoalkane carboxylic acids.

$$\begin{array}{c} RO \\ RO \end{array}\!\!>\!\!P\!-\!(CH_2)_n\!-\!C\!\!<^{O}_{OR'} + PCl_5 \longrightarrow \begin{array}{c} RO \\ Cl \end{array}\!\!>\!\!P\!-\!(CH_2)_n\!-\!C\!\!<^{O}_{OR'} + POCl_3 + RCl$$
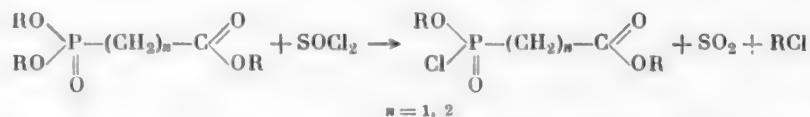
$$n = 0, 1, 2.$$

As a result of the presence of three ester groups in the ester of a phosphonoalkane carboxylic acid this reaction can proceed in a different direction and lead to a mixture of different substances. It was found, however, that the replacement of one ester group in phosphonoalkane carboxylic esters by chlorine as a result of the action of phosphorus pentachloride under specific conditions takes place in a clearly defined manner and with great ease, the various ester groups combined with the phosphorus being replaced with the same degree of ease: OCH_3, OC_2H_5, OC_3H_7-iso, OC_4H_9-n, OC_5H_{11}-iso; the yield of monoacyl chlorides is 60-85%.

The monoacyl chlorides of esters of phosphonoformic acid are also obtained in good yield by the chlorination of a mixture of phosphorus trichloride and the medium ester of phosphonoformic acid by chlorine in an inert solvent. In this case phosphorus pentachloride is formed during the process of chlorination.

Employing these methods we obtained twelve P-acyl chlorides of dialkyl esters of phosphonoformic, phosphonoacetic and phosphonopropionic acids and also the acyl chloride of diethyl thiophosphonopropionate.

The monoacyl chlorides of diethyl phosphonoacetate were also obtained by the action of thionyl chloride on the medium esters.

$$\begin{array}{c} RO \\ RO \end{array}\!\!>\!\!P\!-\!(CH_2)_n\!-\!C\!\!<^{O}_{OR} + SOCl_2 \longrightarrow \begin{array}{c} RO \\ Cl \end{array}\!\!>\!\!P\!-\!(CH_2)_n\!-\!C\!\!<^{O}_{OR} + SO_2 + RCl$$

$$n = 1, 2$$

The acyl chlorides of dialkyl esters of phosphonoalkane carboxylic acids are colorless mobile liquids with a pungent odor, soluble in organic solvents and hydrolyzed by water. The constants of the compounds obtained are given in Table 2.

•Phosphono = dihydroxyphosphinyl. (Translator's note).

The monoacyl chlorides of dialkyl esters of phosphonoalkane carboxylic acids are P-acyl chlorides, i.e. the chlorine atom in them is combined with phosphorus. The position of the chlorine is proven, firstly, by the data of the ultimate analysis on the chlorine of monoacyl chlorides, obtained from dibutyl-C-ethyl and diisopropyl-C-ethyl esters of phosphonopropionic acid and diisopropyl-C-ethyl, dibutyl-C-ethyl and diisoamyl-C-ethyl esters of phosphonoacetic acid, which corresponded to the values calculated for the P-monoacyl chlorides of the corresponding dialkyl esters of phosphonopropionic and phosphonoacetic acids. The P- and C-monoacyl halides of diesters of phosphonoalkane carboxylic acids, obtained from medium esters with unlike ester groups at the phosphorus and carbon atoms will, naturally, be different in composition. In the second place, the position of the chlorine is proven by a comparison of the amides obtained from the monoacyl chlorides of diethyl esters of phosphonoformic and phosphonoacetic acids by replacement of the chlorine by an amide group, with C-amides of diethyl esters of these acids, obtained from medium esters and ammonia [1,2]. The replacement of chlorine in the indicated acyl chlorides was carried out by the action of the theoretical amount of a solution of ammonia in benzene, sufficient to replace only one atom of chlorine. Mixed melts of the samples obtained with the C-amides of diethyl esters of the corresponding phosphonoformic and phosphonoacetic acids showed a depression of the melting point.

TABLE 1

Medium Esters of Phosphonoformic and Phosphonopropionic Acids

Formula	Yield (%)	Boiling point (pressure in mm)	d_1	n_D
$(CH_3O)_2P(O)COOCH_3$	24	87—88° (2)	1.2327 (at 21.5°)	1.4220 (at 21.5°)
$(n-C_4H_9O)_2P(O)COOC_4H_9-n$	81	166.5—167.5 (5)	1.0188 (at 20.5°)	1.4350 (at 20.5°)
$iso-C_3H_7O)_2P(O)CH_2-CH_2-COOC_2H_5$	68	115—117 (2—3)	1.0651 (at 20°)	1.4340 (at 20°)
$(n-C_4H_9O)_2P(O)CH_2CH_2COOC_2H$	81	162—164 (4)	1.0337 (at 20°)	1.4380 (at 20°)

The medium esters of phosphonoalkane carboxylic acids were obtained by known methods [1-3]; together with the esters described in literature four esters of phosphonoformic and phosphonopropionic acids, not described hitherto, were obtained; the properties of the latter are given in Table 1.

EXPERIMENTAL

Reactions of medium esters of phosphonoalkane carboxylic acids with phosphorus pentachloride. 0.21 mole of finely ground phosphorus pentachloride was added slowly in small portions with constant stirring and water-cooling to a solution of 0.2 mole of the medium ester ester of phosphonoalkane carboxylic acid in an equal volume of dry carbon tetrachloride the mixture was then stirred for 15-30 minutes at 18° and for 20-40 minutes at 30-50°. The unreacted phosphorus pentachloride was decomposed by passing dry sulfur dioxide into the mixture at 18°. The carbon tetrachloride, thionyl chloride and phosphorus oxychloride were then distilled off under vacuum and the residue was twice-fractionated. Before it was fractionated, to obtain greater purification from volatile admixtures the residue was sometimes mixed with dry carbon tetrachloride (10-15 ml each time),which was then distilled off under vacuum. The yields and the analytical data of the acyl chlorides obtained by the indicated method are given in Table 2.

The P-amide of diethyl phosphonoformate. 88 ml of a benzene solution of ammonia (concentration 4.04· $\cdot 10^{-3}$ g/ml) was added to a solution of 2.0 g of the freshly distilled appropriate acyl chloride in 25 ml of dry benzene, the mixture being cooled by cold water. After the reaction mixture had been kept in a closed vessel at 18° for a day the ammonium chloride was filtered and the benzene was distilled from the filtrate on a water bath. After the residue had been recrystallized 3 times from a mixture of alcohol and benzene 0.78 g of lustrous

plates with an m.p. of 137° was obtained. A sample of a mixture with the C-amide of diethyl phosphonoformate, obtained from the triethyl ester and ammonia and melting at 133°, melted at 103-104°.

Found % N 7.95, 7.86. $C_5H_{12}O_4NP$. Calculated %: N 7.73.

TABLE 2

Monoacyl Chlorides of Dialkyl Esters of Phosphonoalkane Carboxylic Acids

Formula	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Chlorine content (%)		Yield (%)
				Found	Calcu-lated	
$(CH_3O)ClP(O)COOCH_3$ •	85—86° (1)	1.4167	1.4475	20.80	20.60	63
$(C_2H_5O)ClP(O)COOC_2H_5$ •	107—108 (5)	1.2410	1.4385	17.90	17.68	82
$(n-C_3H_6O)ClP(O)COOC_3H_5$	98—101 (0.35)	1.1977	1.4387	15.45	15.51	81
$(n-C_4H_9O)(Cl)P(O)COOC_4H_9\text{-}n.$	133—134 (3—4)	1.1326	1.4455	13.80	13.82	56
$(C_2H_5O)(Cl)P(O)CH_2COOC_2H_5$ ••	110—111 (3)	1.2584	1.4476	16.59	16.53	84
$(iso\text{-}C_3H_7O)(Cl)P(O)CH_2COOC_2H_5$	92—93 (0.25)	1.1947	1.4430	15.56	15.51	58
$(iso\text{-}C_5H_{11}O)(Cl)P(O)CH_2COOC_3H_5$	110—112 (0.03)	1.1384	1.4463	13.72	13.81	63
$(n-C_4H_9O)(Cl)P(O)CH_2COOC_5H_5$	120—122 (0.35)	1.1551	1.4440	14.46	14.61	68
$(CH_3O)(Cl)P(O)CH_2CH_2COOCH_3$	92—94 (0.2)	1.3306	1.4506	18.00	17.68	80
$(C_2H_5O)(Cl)P(O)CH_2CH_2COOC_2H_5$	101—102 (0.1)	1.2502	1.4555	15.48	15.51	81
$(iso\text{-}C_3H_7O)(Cl)P(O)CH_2CH_2COOC_2H_5$	113—116 (0.05)	1.2352	1.4486	15.08	14.61	80
$(n-C_4H_9O)(Cl)P(O)CH_2CH_2COOC_5H_5$	128—133 (0.05)	1.1526	1.4520	13.97	13.81	74
$(C_2H_5O)(Cl)P(S)CH_2CH_2COOC_2H_5$ •••	118—119 (1)	1.2207	1.4621	14.29	14.49	78

•Found % : P 15.82. Calculated % : P 15.46.

••Found % : C 33.23; H 6.16; P 14.15. Calculated % : C 33.51; H 5.91; P 14.43.

•••Found % : C 34.39; H 6.26; P 12.34; S 12.85. Calculated % : C 34.37; H 5.77; P 12.66; S 13.10.

The P-amide of diethyl phosphonoacetate. 1.5 g of the appropriate acyl chloride was taken in 25 ml of dry benzene and 62 ml of a benzene solution of ammonia (concentration $4.04 \cdot 10^{-3}$ g/ml). The reaction was carried out as described above. After the precipitate had been recrystallized twice from a mixture of benzene and petroleum ether fine white crystals with an m.p. of 103°, soluble in benzene and alcohol and insoluble in petroleum ether, were obtained. A sample of a mixture of the amide obtained and the C-amide of diethyl phosphonoacetate • melted at 60-61°.

Found % : N 7.13, 7.36. $C_6H_{14}O_4NP$. Calculated %: N 7.18.

The P-acyl chloride of dimethyl phosphonoformate. Dry chlorine was passed through a solution of 31 g of trimethyl phosphonoformate and 25.4 g of phosphorus trichloride in 100 ml of carbon tetrachloride, the mixture being cooled with ice and salt and stirred constantly; the rate at which the chlorine was passed was such that the temperature in the flask did not exceed +5°; a precipitate of phosphorus pentachloride was deposited during this process. After chlorination for 30 minutes the mixture was heated for 30 minutes to 40°; this resulted in the precipitate going into solution. The chlorination and heating of the mixture were repeated until the trivalent phosphorus was completely oxidized and was completed after 3 hours. After the carbon tetrachloride and phosphorus oxychloride had been distilled off the residue was distilled twice under vacuum. The yield was 20 g (63%).

B.p. 85-86° (1 mm), d_4^{20} 1.4167, n_D^{20} 1.4475.

Found % Cl 20.8. $C_3H_6O_4PCl$ Calculated %: Cl 20.6.

• The C-amide of diethyl phosphonoacetate, obtained by the action of a concentrated aqueous solution of ammonia on triethyl phosphonoacetate, has an m.p. of 78-80° [1,2] after recrystallization from benzene.

When heated above 170-180° the acyl chloride decomposed with the formation of gaseous products which reduced palladium chloride to the metal; the residue in the flask was tar.

The P-acyl chloride of diethyl phosphonoformate. A solution of 32.1 g of triethyl phosphonoformate and 21 g of phosphorus trichloride was chlorinated for 5 hours, as described above. To remove excess phosphorus pentachloride dry sulfur dioxide was passed into the reaction mass for 20 minutes. After the carbon tetrachloride, thionyl chloride and phosphorus oxychloride had been distilled off the residue was distilled twice under vacuum. The yield was 21.5 g (70 %).

B.p. 107-108° (5 mm), d_4^{20} 1.2410, n_D^{20} 1.4385.

Found %: P 15.60, 16.04; Cl 17.40, 18.00. $C_5H_{10}O_4PCl$. Calculated %: P 15.46; Cl 17.69.

The P-acyl chloride of di-N-butyl phosphonoformate. A solution of 49.8 g of the ester and 23.2 g of phosphorus trichloride in 120 ml of carbon tetrachloride was chlorinated for 6 hours, as described above. After the carbon tetrachloride and phosphorus oxychloride had been distilled off the residue was distilled twice under vacuum. 24.5 g (56.6%) of the acyl chloride was obtained.

B.p. 133-134° (3-4 mm) d_4^{20} 1.1326, n_D^{20} 1.4455.

Found %: C 42.03, 42.46; H 7.29, 7.06; Cl 13.80, 13.58. $C_9H_{18}O_4PCl$. Calculated %: C 42.11; H 7.06; Cl 13.82.

When heated above 190-200° the acyl chloride decomposed with the liberation of gaseous products and the formation of a tarry residue.

The P-acyl chloride of diethyl phosphonoacetate. A mixture of 5.0 g of triethyl phosphonoacetate and 7.95 g of thionyl chloride was heated for 9 hours at 80-90°. The excess thionyl chloride was then distilled off and the residue was kept for 30 minutes under vacuum (11 mm) while heated on a water bath. As a result of distillation 1.95 g of a yellowish liquid, with a b.p. of 94-105° (1 mm), was obtained; the residue in the flask was tar. As a result of repeated distillation 1.58 g (33%) of the acyl chloride was obtained.

B.p. 99-101° (1 mm), n_D^{20} 1.4474.

Found %: Cl 16.66, 16.87. $C_6H_{12}O_4PCl$. Calculated %: Cl 16.53.

The P-acyl chloride of dimethyl phosphonopropionate. 2.1 g of thionyl chloride was added dropwise to 3.0 g of trimethyl phosphonopropionate; as a result the temperature of the mixture rose to 40-50°. The mixture was heated for 1 hour at 80° and for 30 minutes on a boiling water bath; it was then kept under a vacuum of 10 mm at 50-60°. When the residue was distilled under high vacuum,1.65 g of a fraction with a b.p. of 87-96° (0.05mm) was obtained; after repeated distillation 1.25 g (42%) of the acyl chloride was obtained.

B.p. 87-90° (0.04 mm), n_D^{20} 1.4509.

Found %: Cl 18.18, 17.86. $C_5H_{10}O_4PCl$. Calculated %: Cl 17.78.

The P-acyl chloride of diethyl thiophosphonopropionate. 23.4 g (78%) of the acyl chloride was obtained in the form of a colorless liquid with an unpleasant odor, after two distillations, from 31 g of triethyl thiophosphonopropionate and 21.1 g of phosphorus pentachloride under the conditions described above. On hydrolysis with solutions of alkalis the acyl chloride split off sulfur, which interferes with the determination of chlorine by the Volhard method. The chlorine content was determined by the Carius method after combustion.

B.p. 118-119° (1 mm), 123-125° (2 mm), d_4^{20} 1.2207, n_D^{20} 1.4621.

Found %: C 34.48, 34.29; H 6.29, 6.23; P 12.41, 12.27; S 12.80, 12.90; Cl 14.20, 14.38. $C_7H_{14}O_3PSCl$. Calculated %: C 34.37; H 5.77; P 12.66; S 13.10; Cl 14.49.

SUMMARY

1. The P-acyl chlorides of dialkyl esters of phosphonoformic, phosphonoacetic, phosphono- and thiophosphonopropionic acids were obtained by reacting phosphorus pentachloride with medium esters of phosphonoalkane carboxylic acids. It was shown that the P-acyl chorides of dialkyl esters of phosphonoformic acid are also obtained by the reaction of phosphorus trichloride as chlorine with esters of this acid.

2. It was established that when medium esters of phosphonoalkane carboxylic acid react with thionyl chloride only the mono-P-acyl chlorides of dialkyl esters of these acids are obtained.

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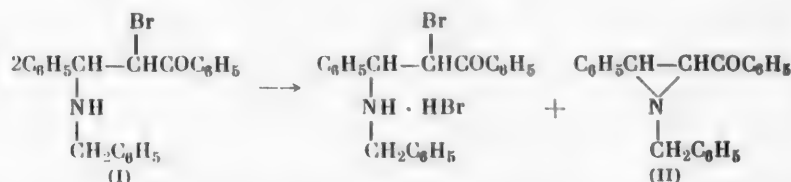
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THE REACTION OF AMINES WITH METHYL α-BROMOACRYLATE
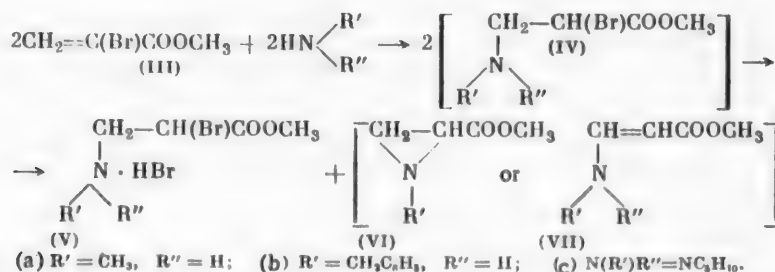# THE SYNTHESIS OF SOME DERIVATIVES OF α-BROMO-β-AMINO ACIDS

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In 1943 Cromwell and his co-workers [1] showed that α-bromo-β-phenyl-β-benzylaminopropiophenone (I) undergoes disproportionation, forming the hydrobromide of α-bromo-β-phenyl-β-benzylaminopropiophenone and 1-benzyl-2-phenyl-3-benzoylethylene imine (II) on standing in benzene solution.

$$2C_6H_5CH-\overset{\overset{\displaystyle Br}{|}}{C}HCOC_6H_5 \longrightarrow C_6H_5CH-\overset{\overset{\displaystyle Br}{|}}{C}HCOC_6H_5 + C_6H_5CH-CHCOC_6H_5$$

We considered it of interest to use this reaction for the synthesis of both the hydrobromides of α-bromo-β-amino acids (compounds which have been very little studied hitherto [2-4]) and the corresponding derivatives of ethylene imine carboxylic acids.

For this purpose we investigated the reaction of methyl α-bromoacrylate (III) with equimolecular amounts of methylamine, benzylamine and piperidine, which, as had been supposed must take place according to the system

$$2CH_2=C(Br)COOCH_3 + 2HN\underset{R''}{\overset{R'}{<}} \longrightarrow 2\left[\underset{R'\quad R''}{\overset{CH_2-CH(Br)COOCH_3}{\underset{|}{N}}}\right] \longrightarrow$$

$$\longrightarrow \underset{R'\quad R''}{\overset{CH_2-CH(Br)COOCH_3}{\underset{|}{N}}} \cdot HBr + \left[\underset{R'}{\overset{CH_2-CHCOOCH_3}{\underset{|}{N}}} \text{ or } \underset{R'\quad R''}{\overset{CH=CHCOOCH_3}{\underset{|}{N}}}\right]$$

(a) R'=CH₃, R''=H; (b) R'=CH₂C₆H₅, R''=H; (c) N(R')R''=NC₅H₁₀.

When a solution of methylamine in dry ether was allowed to act on (III) the expected hydrobromide of methyl α-bromo-β-methylaminopropionate (Va) was precipitated immediately after the evaporation of the solvent. As a result of the reaction of (III) with benzylamine, an oil, which crystallized with only gentle heating (40-50°), was obtained after the evaporation of the ether. The hydrobromide of methyl α-bromo-β-benzylaminopropionate (Vb) was obtained from the reaction mixture. When piperidine acted on (III) the hydrobromide of methyl α-bromo-β-piperidinopropionate (Vb) was only formed when the oil obtained after the evaporation

of the ether was boiled in benzene solution. In all cases the hydrobromides of the corresponding initial amines were obtained as by-products.

It should be noted that the ratios of the hydrobromides of benzylamine and (Vb) depend on the temperature at which the initial reagents are mixed. The optimum yield of (Vb), namely 72% with respect to bromine, is obtained at 20-25°. In this case the yield of benzylamine hydrobromide is about 18%. The composition of the compounds we obtained (Va, b,c) agrees well with the analytical data. An investigation of the infrared spectrum of (Vb) showed the presence of the characteristic frequencies [5]: $\overset{+}{N} - H$ 2720 and 2600 cm^{-1}, C=O 1718 cm^{-1}, C_6H_5 1557 cm^{-1}, CH_2 1447 cm^{-1}, O=C—O 1240 cm^{-1}.

To prove the α-location of the bromine atoms in the molecules of (Va, b,c) we used the method of determining the mobile α-halogen by the liberation of I_2 from an acidified solution of KI in acetone [6,7]. It is known [6] that under these conditions, in contrast to esters of β-halogen acids, esters of α-halogen acids liberate I_2 quantitatively. We obtained satisfactory agreement of the analytical results with the data calculated from the content of the α-bromine atom in (Va, b,c).

According to the system of formation of (V) it was to be expected that compounds of type (VI) or the corresponding derivatives of β-aminoacrylic acid (VII) would be obtained together with (V). We did not succeed, however, in isolating any compound of these types. Attempts to isolate the intermediate base (IV) in pure form were also unsuccessful. The formation of substances of type (VII), not (VI), as a result of the disproportionation of (IV) appears more probable to us because compounds of the (VI) type cannot be obtained in the case of the reaction of (III) with secondary amines (piperidine). As is known [8,9], compounds of type (VII) are very unstable and are readily transformed under the experimental conditions. It must be emphasized, however, that the problem of the formation of (VI) or (VII) requires further investigation.

The formation of the hydrobromides of the initial amines together with (V) can be explained by the presence of unreacted amine in the reaction mixture, this amine combining with the hydrogen bromide split off during the disproportionation of (IV).

The structure (of little probability, in our opinion) of the hydrobromide of methyl α-bromo-α-benzylaminopropionate (VII) is also not contradictory to the analytical data of (Vb), the infrared spectrum and the results of determination of the mobile bromine. This ester (VIII) cannot be formed, however, by the action of HBr on the corresponding 2-carbomethoxyethylene imine (VI, R = $CH_2C_6H_5$) [10] a substance identical with (Vb) is obtained; this was indicated by the absence of a depression of the melting point and the identity of the infrared spectra.

$$\begin{array}{c} Br \\ | \\ CH_3{-}C{-}COOCH_3 \\ | \\ NH \cdot HBr \\ | \\ CH_2C_6H_5 \\ \text{(VIII)} \end{array}$$
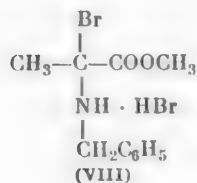
It is interesting to note that when Wagner-Jauregg and his co-workers [10] allowed a solution of HCl in acetone to act on 1-benzyl-2-carbomethoxyethylene imine they obtained the hydrochloride of methyl α-benzylamino-β-chloropropionate. This type of rupture of a three-membered ring, which is contradictory to our data, may possibly be associated with different reaction conditons.

We wish to express our deep appreciation to Yu. I. Sheinker and E. M. Pereslen', who determined and interpreted the infrared spectra, and also to A. Ya. Berlin for his valuable help.

EXPERIMENTAL

The hydrobromide of methyl α-bromo-β-methylaminopropionate (Va). 10 ml of a solution of 0.6 g of CH_3NH_2 in dry ether was added to a solution of 3.32 g of (III) [11] in 20 ml of dry ether at 20°, for 15 minutes. The mixture was stirred for 1 hour at 18-20°, it was filtered from the precipitated methylamine hydrobromide and the ether was evaporated under vacuum. The solid residue obtained was treated with 70 ml of dry hot $CHCl_3$, it was filtered from methylamine hydrobromide and the chloroform solution was left for a day to crystallize. The precipitate formed was separated and washed with cold $CHCl_3$. The yield was 0.9 g, the m.p. was 115-117°. After evaporation and treatment with ether a further 0.25 g of the substance, with an m.p. of 115-118°, was obtained from the filtrate. The total yield of (Va) was 43% (according to the bromine). For purposes of analysis the product was crystallized from an ethanol-hexane mixture (1:1) and then twice-recrystallized from an ethyl acetate-methanol mixture (4:1); the m.p. was 122.8-123.3° (with decomp.). *

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*All the melting points are corrected.

Found % C 21.79; H 3.94; N 4.98; Br (ionic) 29.19; Br (total) 57.81; Br_a 28.31. $C_5H_{11}O_2NBr_2$. Calculated%
C 21.68; H 4.00; N 5.05; Br (ionic)28.87; Br (total) 57.75; Br_a 28.87.

The total yield of methylamine hydrobromide was 0.14 g, the m.p. was 249-250°; the melting point of a mixed sample was 249-250°.

The hydrobromide of methyl α-bromo-β-benzylaminopropionate (Vb). a) 1.05 g of (III) in 15 ml of dry ether was mixed with 0.67 g of benzylamine under the conditions described for (Va). The oil obtained after the ether had been evaporated was heated on a water bath to 45-50° and kept at this temperature for 15-20 minutes. The solidified mass was treated with 20 ml of dry $CHCl_3$, filtered and the filtrate evaporated to dryness under vacuum. The solid residue was mixed with 30 ml of dry ether and filtered. The yield of (Vb) was 0.8 g (72%), the m.p. was 135-137°. For purposes of analysis the substance was crystallized from ethyl acetate and then twice recrystallized from a 2:1 ethanol-hexane mixture. The m.p. was 142.1-142.6° (with decomp.).

The filtrate from (Vb) was evaporated and an attempt was made to distill the residue under vacuum but this resulted in the decomposition of the substances.

Found %: C 37.43; H 4.34; N 3.78; Br (ionic) 23.33; Br (total) 45 47; Br_a 22.00. $C_{11}H_{15}O_2NBr_2$. Calculated%
C 37.40; H 4.25; N 3.96; Br (ionic) 22.64; Br (total) 45.28; Br_a 22.64.

Infrared spectrum (cm^{-1}): 2940, 2743, 2600, 1718, 1562, 1447, 1396, 1360, 1312, 1183, 1154, 995, 970, 944, 921, 856, 810, 787, 759, 705.

The total yield of benzylamine hydrobromide was 0.12 g (18%), the m.p. was 218-220°; the melting point of a mixed sample was 218-220°.

b) 1.25 g of 1-benzyl-2-carbomethoxyethylene imine (VI, R = $CH_2C_6H_5$) [10] was dissolved in 20 ml of dry ether and while it was cooled with a freezing mixture, a current of dry HBr was passed into the solution until the formation of a precipitate had ceased. The ether was decanted and the residue was dissolved in 10 ml of $CHCl_3$, the solution was boiled with activated charcoal, filtered and the solvent was evaporated under vacuum. After it had stood in a refrigerator, the solid product was triturated with ether and filtered. The weight was 1.8 g (78%). After crystallization from ethyl acetate and then from a mixture of ethanol and hexane the substance melted at 142.5-143° (with decomp.). A mixed sample with the substance obtained in experiment "a" melted at 142-143° (with decomp.).

Found %: C 37.78; H 4.27; N 3.57; Br (ionic) 23.54; Br (total) 45.48; Br_a 22.07. $C_{11}H_{15}O_2NBr_2$.
Calculated %: C 37.43; H 4.25; N 3.96; Br (ionic) 22.64; Br (total) 45.28; Br_a 22.64.

Infrared spectrum (cm^{-1}): 29 40, 2723, 2600, 1718, 1557, 1447, 1392, 1357, 1306, 1181,1152,994,969,942, 920,856,810,787,758,705.

The hydrobromide of methyl α-bromo-β-piperidinopropionate (Vb). 2.8 g of (III) and 1.66 ml of piperidine were mixed in a solution of dry ether, as described for (Va). The oil obtained after the ether had been evaporated was dissolved in 20 ml of dry benzene and filtered from piperidine hydrobromide (0.2 g, m.p.235°; melting point of a mixed sample 235°); the solution was then heated to boiling and boiled for 1.5 hours. The solution was cooled, the precipitate was filtered and washed with benzene and petroleum ether. The yield of (Vb) was 2.45 g (88%), the m.p. was 155-157°. For purposes of analysis the product was crystallized twice from a mixture of methanol and ether (3:2), the m.p. was 159.5-160° (with decomp.).

Found %: C 32.53; H 5.14; N 4.20; Br (ionic) 25.21; Br (total) 48.10; Br_a 23.63. $C_9H_{17}O_2NBr_2$. Calculated %: C 32.65; H 5.17; N 4.23; Br (ionic) 24.12; Br (total) 48.24; Br_a 24.12.

SUMMARY

1. It was found that when equimolecular amounts of methylamine, benzylamine or piperidine react with methyl α-bromoacrylate the corresponding hydrobromides of methyl α-bromo-β-alkylaminopropionates are formed.

2. The hydrobromides of the methyl esters of α-bromo-β-methylamino- and α-bromo-β-benzylamino- and α-bromo-β-piperidino propionic acids, not described hitherto in literature, were synthesized with yields of

43, 72 and 88% according to bromine), respectively. The structure of the compounds obtained was confirmed by the quantitative determination of the α-bromine atom.

3. The hydrobromide of methyl α-bromo-β-benzylaminopropionate was also obtained by the action of dry HBr on 1-benzyl-2-carbomethoxyethylene imine.

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SYNTHESIS AND PROPERTIES OF DIMERCAPTO DERIVATIVES OF ALKANE SULFONIC ACIDS

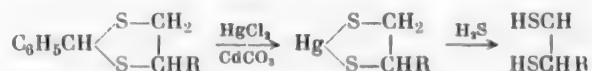## V. SODIUM 1,3-DIMERCAPTOPROPANE-2-SULFONATE *

V. E. Petrun'kin and N. M. Lysenko

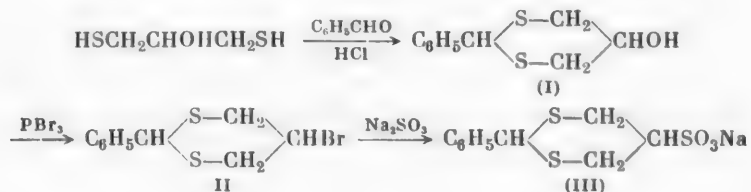Ukraine Scientific-Research Sanitary-Chemical Institute

One of us has previously [2] described the synthesis of sodium 2,3-dimercaptopropanesulfonate (unithiol), used in medicine as an antidote for compounds of arsenic, mercury and a number of other heavy metals. Sodium 1,3-dimercaptopropane-2-sulfonate (isounithiol), isomeric with unithiol, was hitherto unknown. In view of its structural similarity with α-lipoic acid, which plays an important part in exchange processes of the organism[3], isounithiol and its disulfide are of interest as a possible model for the former.

Like unithiol and other 1,2-dimercaptosulfonates synthesized by us [1], isounithiol can evidently be obtained by an exchange reaction of the corresponding dibromide, i.e. sodium 1,3-dibromopropane-2-sulfonate, with KSH. However, in view of the difficulty of obtaining the dibromide itself we rejected this method of synthesis.
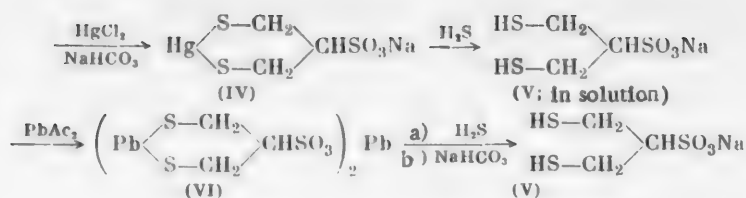
In order to obtain the isomer of unithiol we used the method developed by Hach [4] for the synthesis of certain 1,2-dithiols. The method considered the conversion of derivatives of 2-phenyl-1,3-dithiolan into 1,2-dithiols by means of mercuric chloride in the presence of cadmium carbonate.

$$C_6H_5CH\begin{array}{c}S-CH_2\\ |\\ S-CHR\end{array} \xrightarrow[CdCO_3]{HgCl_2} Hg\begin{array}{c}S-CH_2\\ |\\ S-CHR\end{array} \xrightarrow{H_2S} \begin{array}{c}HSCH\\ |\\ HSCHR\end{array}$$

According to our observations, derivatives of 2-phenyl-1,3-dithian react in an analogous manner with mercuric chloride. In this process 1,3-dithiols are obtained with a satisfactory yield if the rupture of the dithian ring by mercuric chloride is carried out in the presence of sodium bicarbonate. In accordance with this, the synthesis of sodium 1,3-dimercaptopropane-2-sulfonate was carried out on the basis of 1,3-dithioglycerin by a method employing the following conversions.
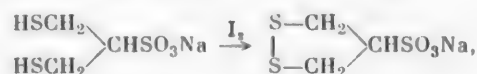
$$HSCH_2CHOHCH_2SH \xrightarrow[HCl]{C_6H_5CHO} C_6H_5CH\begin{array}{c}S-CH_2\\ \\ S-CH_2\end{array}CHOH$$
(I)

$$\xrightarrow{PBr_3} C_6H_5CH\begin{array}{c}S-CH_2\\ \\ S-CH_2\end{array}CHBr \xrightarrow{Na_2SO_3} C_6H_5CH\begin{array}{c}S-CH_2\\ \\ S-CH_2\end{array}CHSO_3Na$$
II   (III)

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*See paper IV [1].

$$\xrightarrow[\text{NaHCO}_3]{\text{HgCl}_2} \quad \text{Hg}\underset{\text{S—CH}_2}{\overset{\text{S—CH}_2}{\Big\langle}}\text{CHSO}_3\text{Na} \xrightarrow{\text{H}_2\text{S}} \underset{\text{HS—CH}_2}{\overset{\text{HS—CH}_2}{}}\text{CHSO}_3\text{Na}$$

(IV)   (V; in solution)

$$\xrightarrow{\text{PbAc}_2} \left(\text{Pb}\underset{\text{S—CH}_2}{\overset{\text{S—CH}_2}{\Big\langle}}\text{CHSO}_3\right)_2\text{Pb} \xrightarrow[\text{b) NaHCO}_3]{\text{a) H}_2\text{S}} \underset{\text{HS—CH}_2}{\overset{\text{HS—CH}_2}{}}\text{CHSO}_3\text{Na}$$

(VI)   (V)

    2-Phenyl-5-hydroxy -1,3-dithian (I) [5] was obtained by the condensation of 1,3-dithioglycerine with benzaldehyde; by means of PBr$_3$ the former was converted to 2-phenyl-5-bromo-1,3-dithian (II). Replacement of the bromine in 2-phenyl-5-bromo-1,3-dithian by a sulfonic group took place smoothly by heating this mono-bromide with an aqueous solution of sodium sulfate; as a result sodium 2-phenyl-1,3-dithian-5-sulfonate (III) was obtained with a good yield. By heating with an aqueous solution of mercuric chloride in the presence of NaHCO$_3$ it was converted to sodium 1,3-mercurodimercaptopropane-2-sulfonate (IV). The subsequent splitting off of the mercaptide mercury in alcohol by hydrogen sulfide gave an alcoholic solution of the sodium salt of 1,3-dimercaptopropane-2-sulfonic acid (V), which, as in the preparation of unithiol, was converted by means of lead acetate to the difficultly soluble Pb salt (VI). As a result of the decomposition of this salt by hydrogen sulfide in alcohol an alcoholic solution of 1,3-dimercaptopropane-2-sulfonic acid was obtained. When neutralized by soda, isounithiol was precipitated from the solution in the form of colorless crystals.

    The isomeric structure, with respect to unithiol, of this sodium dimercaptopropanesulfonate is confirmed by a certain difference in their properties. For example, isounithiol is more difficultly soluble in water and alcohol than unithiol. The S-benzylthiuronium salts (VII), obtained from the products of the reaction of iso-unithiol with PbO, ZnO, HgO, benzaldehyde and acetophenone, have lower melting points (except the Pb salt) than the corresponding salts (VIII) in the unithiol series (see table) : BT = cation of S-benzylthiuronium).

    When isounithiol is oxidized by iodine it is converted to the corresponding cyclic disulfide, sodium 1,2-dithiolan-4-sulfonate characterized in the form of the S-benzylthiuronium salt. The latter melted considerably lower (90-92°) than the benzylthiuronium salt obtained from the oxidation product of unithiol (177-178°) [2].

    Isounithiol forms stabler complexes than unithiol with certain heavy metals.

$$\underset{\text{HSCH}_2}{\overset{\text{HSCH}_2}{}}\text{CHSO}_3\text{Na} \xrightarrow{\text{I}_2} \underset{\text{S—CH}_2}{\overset{\text{S—CH}_2}{\Big|}}\text{CHSO}_3\text{Na},$$

S-Benzylthiuronium Salts of Derivatives of Isounithiol and Unithiol

A	General formula	Calculated % N	A$\underset{\text{S—CH}_2}{\overset{\text{S—CH}_2}{\Big\langle}}$CHSO$_3$BT (VII)		A$\underset{\text{S—CHCH}_2\text{SO}_3\text{BT}}{\overset{\text{S—CH}_2}{\Big\langle}}$ (VIII)	
			% N found	Melting point	% N found	Melting point
Pb	C$_{11}$H$_{16}$O$_3$N$_2$S$_4$Pb	5.01	4.69, 4.66	162°	—	152° [6]
Zn	C$_{11}$H$_{16}$O$_3$N$_2$S$_4$Zn	6.71	6.91, 7.09	155	—	164 [6]
Hg	C$_{11}$H$_{16}$O$_3$N$_2$S$_4$Hg	5.07	5.40, 5.47	128—129	—	150 [6]
				Temp. decomp.		Temp. decomp.
C$_6$H$_5$CH	C$_{18}$H$_{22}$O$_3$N$_2$S$_4$	6.33	6.49, 6.61	99—100	6.27	143—144
C$_6$H$_5$CCH$_3$	C$_{19}$H$_{24}$O$_3$N$_2$S$_4$	6.14	6.39, 6.42	150	6.34, 6.14	170

EXPERIMENTAL

<u>1,3-Dithioglycerin</u> was obtained in the form of its Pb salt. Glycerin dichlorohydrin (62.5 g) was digested

with an alcoholic solution of KSH (from 100 g of KOH in 450 ml of alcohol) for 6 days at room temperature (23-26°). The precipitate of KCl was separated. 35.1 g (58.5%) of dithiol was found iodometrically in the filtrate (after acidification with acetic acid to Congo and removal of hydrogen sulfide by injection of CO_2). The filtrate was poured into a solution of lead acetate (1 38 g in 500 ml of water). The precipitate of lead mercaptide was washed repeatedly on the filter with hot water (4 liters). 83.9 g of the Pb salt of 1,3-dithioglycerin , with a purity of 97% (iodometric titration in 10% H_2SO_4) was obtained.

Found %: Pb 63.70. $C_3H_{60}S_2Pb$. Calculated % Pb 62.93.

2-Phenyl-5-hydroxy-1,3-dithian (I). 80 g of the finely crushed Pb salt of 1,3-dithioglycerin was well mixed with a 15% alcoholic solution of HCl (200 ml), the precipitate was separated and again mixed with the same solution (100 ml). 29.2 g of dithiol (97%, calculated on the Pb salt) was found in the filtrate from both treatments of the precipitate). The alcoholic solution of 1,3-dithioglycerin , containing HCl, obtained was mixed with benzaldehyde (25 g). The next day the solution was poured into ice water (600 ml). The precipitate of 2-phenyl-5-hydroxy-1,3-dithian deposited was washed with water and dried over $CaCl_2$. The yield was 43.5 g (87%). It was in the form of colorless crystals with an m.p. of 115° (from benzene), literature data [5]: m.p. 142-143°.

Found %: S 31.00. $C_{10}H_{12}OS_2$ Calculated %: S 30.22.

2-Phenyl-5-bromo-1,3-dithian (II). PBr_3 (19.4 g) was added gradually with cooling to 2-phenyl-5-hydroxy-1,3-dithian (43 g). The mixture was heated for 1 hour on a water bath. Two layers of liquid were formed. The lower layer was thrown away; the upper (clearer) layer was poured into ice water (300 ml). The precipitate of phenylbromodithian deposited was filtered and washed with water. The yield was 48.1 g (86%). It was in the form of colorless needles with an m.p. of 65-67° (from alcohol). It was obtained for the first time.

Found %: Br 29.45, S 23.57. $C_{10}H_{11}S_3Br$. Calculated %: Br 29.09; S 23.27.

Sodium 2-phenyl-1,3-dithian-5-sulfonate (III). The crude 2-phenyl-5-bromo-1,3-dithian (46 g) was heated with a freshly prepared solution of sodium sulfite (from 21.6 g of soda in 120 ml of water and SO_2) almost to boiling for 1 hour (until the precipitate of bromide had completely disappeared). When it had cooled, sodium 2-phenyl-1,3-dithian-5-sulfonate was precipitated in the form of a colorless crystalline powder. The yield was 42.9 g (79%). It was obtained for the first time. The analysis was carried out after recrystallization from water.

Found %: Na 7.49. $C_{10}H_{11}O_3S_3Na$. Calculated %: Na 7.72.

Sodium 1,3-mercurydimercaptopropane-2-sulfonate (IV; technical product). 35 g of mercuric chloride and 12 of sodium bicarbonate were added for 1 hour in small portions with stirring and heating (bath temperature 60-65°) to a solution of 40 g of crude sodium 2-phenyl-1,3-dithian-5-sulfonate. The solution was then heated for another hour, after which 44.8 g (81%) of sodium mercurydimercaptopropanesulfonate was detected in it iodometrically. The salt was precipitated from the solution by alcohol (500 ml) in the form of the technical product, 72% pure.

Lead 1,3-leaddimercaptopropane-2-sulfonate (VI). 36.8 of the finely crushed technical mercuro-sodium salt of 1,3-dimercaptopropane-2-sulfonic acid was decomposed with hydrogen sulfide in 100 ml of alcohol. After filtration the precipitate was treated with hydrogen sulfide in a fresh amount of alcohol. The hydrogen sulfide was removed from the combined filtrates by a current of CO_2, after which 8.7 g (70%) of sodium 1,3-dimercaptopropane-2-sulfonate was found in the solution. When it was poured into a hot solution of lead acetate (25 g in 120 ml of water) a yellow precipitate of the lead salt was deposited; this was washed on the filter with hot water. The yield was 18.8 g. From the data of an iodometric titration (in 10% H_2SO_4) it was a technical product 80% pure. It contained admixtures of plumbous chloride.

Sodium 1,3-dimercaptopropane-2-sulfonate (V; isounithiol). A current of hydrogen sulfide was passed for about 2 hours through a suspension of 18.7 g of the finely crushed lead salt of 1,3-dimercaptopropane-2-sulfonic acid in 75 ml of alcohol. The black precipitate was separated and was treated again by the same method in 50 ml of alcohol. The filtrates were combined and evaporated until the concentration of the dithiole acid was 15-17% 5.7 g of the dithiole acid was found. The solution was neutralized with sodium bicarbonate while heated on a water bath. After it had cooled 3.9 g of isounithiol was deposited from the solution in the

form of fine plates, 98% pure. It contained one molecule of water of crystallization. After this had been removed (at 70° under vacuum the m.p. was 180-197°; the temp. of decomp. was 220°.

Found %: SH 28.50; Na 10.17; H_2O 7.45. $C_3H_7O_3S_3Na \cdot H_2O$. Calculated %: SH 28.98; Na 10.08; H_2O 7.89.

In addition, a further 2.1 g of impure isounithiol (68% pure) was precipitated from the mother liquor with ether.

The sodium salts of 1,3-lead-,1,3-zinc- and 1,3-mercury-dimercaptopropane-2-sulfonic acid were obtained from isounithiol and lead, zinc and mercuric oxides in the same way as from unithiol, followed by the conversion of the sodium salts to the corresponding S-benzylthiuronium salts [6] (Table 1). The latter were colorless (yellow in the case of Pb) amorphous powders.

Sodium 2-phenyl-1,3-dithiolan-4-methylsulfonate (VIII; A = C_6H_5CH). 2.1 g of benzaldehyde and 3 drops of conc. HCl were added to a solution of 4.6 g of unithiol in 10 ml of water. When the mixture was shaken an exothermic reaction took place. The next day the precipitate of the salt deposited was washed with water, alcohol and ether. The yield was 6.2 g. It was in the form of lustrous plates, moderately soluble in water; the temp. of decomp. was 233-235° (from alcohol).

Found %: Na 7.77. $C_{10}H_{11}O_3S_3Na$. Calculated %: Na 7.71.

Sodium 2-methyl-2-phenyl-1,3-dithiolan-4-methylsulfonate (VIII; A = $C_6H_5CH_3$). This was obtained in a similar manner to the previous product, from unithiol and acetophenone. A precipitate of the salt separated out after the mixture had stood for 4 days. It was in the form of lustrous rectangular plates, moderately soluble in water. The m.p. was 142-145° (from water).

Found %: Na 7.18. $C_{11}O_{13}O_3S_3Na$. Calculated %: Na 7.36.

Attempts to separate the salt into the isomers (cis and trans) by fractional crystallization from alcohol or water were unsuccessful (the S-benzylthiuronium salts, obtained from different fractions of the sodium salts,had the same melting point; the mixtures did not show any depression of the melting point).

Sodium 2-phenyl- and 2-methyl-2-phenyl-1,3-dithian-5-sulfonate (VII; A = C_6H_5CH and $C_6H_5CCH_3$) were obtained in an analogous manner by condensing isounithiol with benzaldehyde and acetophenone, respectively. They were in the form of colorless crystalline powders. They were characterized in the form of the S-benzylthiuronium salts (table).

Sodium 1,2-dithiolan-4-sulfonate. 0.28 g of iodine was added with stirring to a solution of 0.5 g of isounithiol in 2.5 ml of water. The solution obtained was partially evaporated on a water bath. The salt was precipitated with alcohol. The yield was 0.2 g. It was a cream-colored finely crystalline powder. Aqueous solutions of the salt had a yellow color.

Found %: Na 10.64. $C_3H_5O_3S_3Na$. Calculated %: Na 11.05.

The S-benzylthiuronium salt was a finely crystalline powder with a faint-yellow color; the m.p. was 90-92°.

Found %: N 8.07, 8.13. $C_{11}H_{16}O_3N_2S_4$. Calculated %: N 7.95.

SUMMARY

The synthesis of the isomer of unithiol — sodium 1,3-dimercapto-propane-2-sulfonate — and also its oxidation product, sodium 1,2-dithiolan-4-sulfonate, was carried out for the first time by the exchange reaction of 2-phenyl-5-bromo-1,3-dithian with sodium sulfite followed by treatment of the sodium 2-phenyl-1,3-dithian-5-sulfonate formed with mercuric chloride in the presence of soda. Certain derivatives of isounithiol were obtained and characterized.

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# SYNTHESIS AND PROPERTIES OF PYRROLIDINE BASES.

V. ETHYL ETHER OF 5-METHYL-PROLINOL AND ITS N-SUBSTITUTED HOMOLOGS

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Continuing our investigations [1,2], we have carried out the hydroamination of α-ethoxymethyl-γ-aceto-propyl alcohol (I) for the purpose of synthesizing derivatives of 5-methylprolinol and its N-substituted homologs. Some derivatives of this class have considerable physiological activity [3].

In the present communication we describe the preparation of the ethyl ether of 5-methylprolinol and its N-substituted homologs (II) by the hydroamination of α-ethoxymethyl-γ-acetopropyl alcohol with formamide and its N-substituted derivatives.
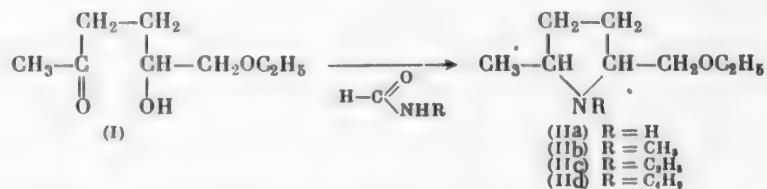
The starting α-ethoxymethyl-γ-acetopropyl alcohol (I) was synthesized by the following scheme:
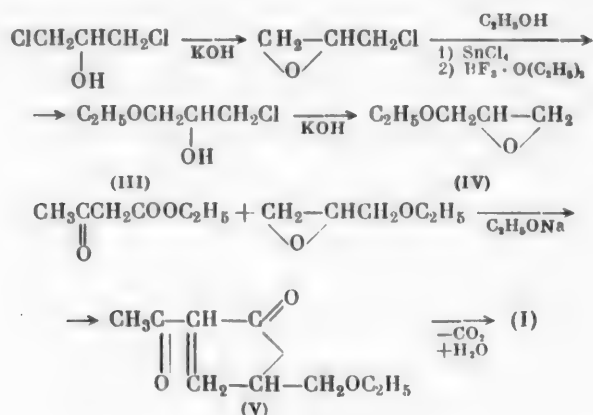
We accomplished the preparation of the ethyl ether of the α-monochlorohydrin of glycerin (III) from epichlorohydrin in the presence of anhydrous stannic chloride [4] or boron fluoride etherate [5].

We carried out the condensation of sodium acetoacetic ester with the ethyl ether of glycidol with some changes in the method published previously [4] that increased the yield of the lactone (V) up to 80% (compared

with 46% indicated by the authors). The lactone (V) was decarboxylated by the method of Vanderwerf [6] with dilute hydrochloric acid.

In the hydroamination of the γ-ketoalcohol we sometimes used the formyl derivative of the amine which had been prepared beforehand, and sometimes (for the ethyl- and butylamine) heated a mixture of the γ-keto-alcohol, amine, and formic acid, which procedure did not lower the yield of the pyrrolidine base.

Introduction of a nickel catalyst [7] into the reaction mixture did not noticeably affect the yield of the pyrrolidine base; however, it permitted an appreciable lowering of the temperature of the hydroamination reaction.

The presence in the pyrrolidine bases prepared by us of two asymmetric centers greatly complicated the separation of the individual compounds. In most cases the picrates and picrolonates of the pyrrolidines obtained were isolated as noncrystallizing oils.

Rather unexpected (but apparently not accidental) for pyrrolidines of such structure was the fact that the molecular refraction was low by approximately two units in comparison with the theoretically calculated value. Cases of exaltation of the molecular refraction had been observed previously for pyrrolidine bases with aromatic substituents on the nitrogen [8].

EXPERIMENTAL

Ethyl ether of the α-monochlorohydrin of glycerin (III). 1. In a four-necked flask fitted with a stirrer, reflux condenser, dropping funnel, and thermometer were placed 300 ml of anhydrous ethyl alcohol, and 6.6 g (5 ml) of anhydrous stannic chloride, and then 92.5 g of epichlorohydrin was introduced in small portions. After half of the epichlorohydrin had been added, a rapid rise in temperature was observed. The temperature of the reaction mixture was kept at 50-60° by cooling. To complete the reaction, the mixture was heated for 30 minutes at the same temperature, then neutralized and fractionated under reduced pressure. 132 g (95% of the ethyl ether of the α-monochlorohydrin of glycerin was obtained.

B.p. 71-72° (12 mm), d_4^{20} 1.1110, n_D^{20} 1.4443, MR_D 33.15; calc. 33.32.

2. To a mixture of 230 ml of anhydrous alcohol and 0.3 ml of boron fluoride etherate cooled to -10° in a three-necked flask with a stirrer, thermometer, and condenser was added 92.5 g of epichlorohydrin in small portions. The reaction proceeded with appreciable evolution of heat. The process was carried out at 50-60°, with cooling. In 4 hours the mixture was fractionated, after the boron fluoride etherate had first been decomposed by treatment with potassium hydroxide. 125 g (84%) of the ethyl ether of the α-monochlorohydrin of glycerin was obtained.

B.p. 71-72° (12 mm), d_4^{20} 1.1117, n_D^{20} 1.4445, MR_D 33.14; calc. 33.32. Literature data [4,5]: b.p. 185-189°, d_4^{15} 1.1247, n_D^{15} 1.4450.

Ethyl ether of glycidol (IV) [6]. 82 g (91%) of the ethyl ether of glycidol was obtained from 72 g of finely ground potassium hydroxide and 124 g of the ethyl ether of the α-monochlorohydrin of glycerin.

B.p. 124-126° (756 mm), d_4^{20} 0.9440, n_D^{20} 1.4075, MR_D 26.00; calc. 26.37. Literature data [6]: b.p. 128-130°, d_4^{25} 0.9554, n_D^{25} 1.4080.

α-Aceto-δ-ethoxy-γ-valerolactone (V) [4]. To 200 ml of anhydrous methyl alcohol placed in a liter three-necked flask (fitted with a stirrer, thermometer, and condenser) was added 18.4 g of metallic sodium. To the sodium methylate obtained was added 104 g of acetoacetic ester, and then 71.4 g of the ethyl ether of glycidol was added at 50°. The reaction mixture was stirred for 6 hours, after which it was allowed to stand overnight. The alcohol was distilled off in vacuo and the residue was neutralized with 10% acetic acid and extracted with ether. The ether extracts were dried with calcined potassium carbonate and fractionated. 90 g (79.5%) of α-aceto-δ-ethoxy-γ-valerolactone was obtained.

B.p. 156-159°, d_4^{20} 0.9036, n_D^{20} 1.4570, MR_D 44.75; calc. 44.87. Literature data [4]: b.p. 159-162° (12 mm), n_D^{25} 1.4566.

α-Ethoxymethyl-γ-acetopropyl alcohol (I) [4]. A mixture of 93 g of (V), 50 ml of concentrated hydrochloric acid, and 250 ml of water was refluxed on a water bath for 5-6 hours until the evolution of carbon dioxide gas ceased. The reaction mixture was saturated with potassium carbonate, extracted with ether, and dried with fused potassium carbonate. After fractionation, 60 g (87.5%) of α-ethoxymethyl-γ-acetopropyl alcohol was obtained.

B.p. 116-117° (10 mm), d_4^{20} 1.021, n_D^{20} 1.4415, MR_D 41.86; calc. 42.22. Literature data [4]: b.p. 124-126° (13 mm), n_D^{25} 1.4412.

Ethyl ether of 5-methylprolinol (IIa). In a distilling flask, provided with a thermometer lowered into the liquid and a receiving vessel, was placed a mixture of 30 g of α-ethoxymethyl-γ-acetopropyl alcohol, 56 g of formamide, and 2 g of powdered nickel. The reaction started at 140° and proceeded with copious evolution of carbon dioxide gas. In 2 hours the temperature rose to 160° and the evolution of carbon dioxide slackened. The reaction mixture was cooled to room temperature, 5 ml of anhydrous formic acid was added, and heating was continued. The reaction again started at 140°. As the evolution of carbon dioxide gas slackened, the addition of formic acid was repeated (for 6-8 hours). Heating was continued for 48 hours. After the reaction mixture had been cooled, 70 ml of conc. HCl and 210 ml of water were added and the mixture was boiled for 6 hours. The reaction product was neutralized with a solution of sodium hydroxide and extracted with ether. The extract was dried with potassium hydroxide and fractionated. 12.7 g (50%) of 2-methyl-5-ethoxymethylpyrrolidine was obtained.

B.p. 115-117° (7 mm), d_4^{20} 0.9640, n_D^{20} 1.4571, MR_D 40.47; calc. 42.19.

Picrate — fine flakes (from alcohol) with m.p. 130-131°.

Found %: N 14.43, 14.25. $C_{14}H_{22}O_8N_4$. Calculated %: N 14.43.

Ethyl ether of 1,5-dimethylprolinol (IIb). In a manner similar to that described above for (IIa), a reaction was carried out with 10 g of α-ethoxy-methyl-γ-acetopropyl alcohol, 20 g of methylformamide, and 1 g of powdered nickel. The mixture was heated for 42 hours at 130-180°, during which 20 ml of anhydrous formic acid was added. After hydrolysis with hydrochloric acid (50 ml conc. HCl in 100 ml of water), the treatment described for (IIa) was carried out. 4 g (40%) of the ethyl ether of 1,5-dimethylprolinol was obtained.

B.p. 114-115° (7 mm), d_4^{20} 0.9425, n_D^{20} 1.4500, MR_D 44.90; calc. 47.14.

Found %: N 8.96, 8.45. $C_9H_{19}ON$. Calculated %: N 8.79.

Ethyl ether of 1-ethyl-5-methylprolinol (IIc). A mixture of 30 g of ethylamine, 63 g of 85% formic acid, 15 g of (I) and 2 g of nickel was heated for 30 hours, at a temperature not above 180°. After this time, 15 ml of anhydrous formic acid was added to the mixture. The reaction product was boiled with 70 ml of concentrated hydrochloric acid and 140 ml of water for 5 hours. After treatment as described above for (IIa), 8 g (50%) of the ethyl ether of 1-ethyl-5-methylprolinol was obtained.

B.p. 108-110° (4 mm), d_4^{20} 0.9266, n_D^{20} 1.4504, MR_D 49.71; calc. 51.76.

Found %: N 7.60, 7.88. $C_{10}H_{21}ON$. Calculated %: N 8.18.

Ethyl ether of 1-butyl-5-methylprolinol (IId). A mixture of 20 g of (I), 42.8 g of butylamine, 45 g of 85% formic acid, and 2 g of powdered nickel was heated for 45 hours at 150-180°. After this time, 25 ml of anhydrous formic acid was added. Further treatment and separation was carried out as described above. 10 g (44.4%) of the ethyl ether of 1-butyl-5-methylprolinol was obtained.

B.p. 120-121° (2 mm), d_4^{20} 0.9115, n_D^{20} 1.4508, MR_D 58.86; calc. 60.99.

Found %: N 6.54, 6.64. $C_{12}H_{25}ON$. Calculated %: N 7.02.

SUMMARY

By hydroamination of α-ethoxymethyl-γ-acetopropyl alcohol with formamide and its N-substituted derivatives, the following compounds were obtained in 40-50% yields: ethyl ether of 5-methylprolinol (IIa), ethyl ether of 1,5-dimethylprolinol (IIb), ethyl ether of 1-ethyl-5-methylprolinol (IIc), and ethyl ether of 1-butyl-5-methyl prolinol (IId).

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METHOD OF INTRODUCING SUBSTITUTENTS INTO THE BENZENE RING OF INDOLE.

II. PREPARATION OF 5-BROMO-1-METHYLINDOLE AND 5-AMINO-1-METHYLINDOLE.

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In the first communication [1] we have described, through the example of 6-nitro-1-methylindole and 6-amino-1-methylindole, a new method for the synthesis of indoles substituted in the benzene ring. The proposed method is essentially as follows: indole (or its homolog) is reduced to the corresponding dihydroindole (indoline), which is an aromatic amine and consequently capable of replacement reactions in the benzene ring. After the introduction of the appropriate substitutent, the indoline is dehydrogenated to the indole.

The first stage of this method — the reduction of indole and its homologs — does not present any difficulties. 1-Methylindole, methylketole, and skatole are easily reduced by the action of zinc or tin in hydrochloric acid [2, 3], and also electrolytically [4]. Dihydroindole is formed in low yield by the electrolytic reduction of indole, but it is obtained in yields up to 90% by the hydrogenation of indole in the presence of Raney nickel at 100° and 100 atm. [5,6].

The second stage — replacement of hydrogen in the benzene ring of the indoles — has been studied comparatively little. By nitration, nitrosation, and azo coupling of dihydromethylketole and dihydroskatole, the corresponding nitro-, nitroso-, and azo-compounds were obtained [3,7] and from them, 5- and 6-aminodihydromethylketole and -skatole were prepared. By diazotization of 6-aminodihydroskatole and 6-aminodihydromethylketole, Braun [7] prepared the corresponding hydroxyindolines. Proof of the position of the substitutents in the indoline nucleus is not cited in his work. With these few references the literature on the problem under consideration is exhausted.

The third step — dehydrogenation of the indolines — has been described in several instances. Julian and Printy [8] dehydrogenated 1-methylindoline by boiling with chloranil in xylene. Woodward et al. [9] prepared lysergic acid by heating dihydrolysergic acid with Raney nickel and sodium arsenate. Of great interest are the publications of Japanese investigators [10-12] who dehydrogenated indoline and tetrahydrocarbazole by the use of platinum black and such hydrogen acceptors as cinnamic acid or safrole. The dehydrogenation of indoline on a Ni — NiCrO$_2$ catalyst at 200° also has been described [13], as well as the preparation of methylketole by distillation of dihydromethylketole over silver sulfate [14, 4].

The proposed method of synthesis of indoles substituted in the benzene ring is based on "temporary shutting off" from reaction of the very active 2,3-positions of indole. In other words, it is possible in this way to avoid up to the last stage those properties, troublesome in connection with the synthesis, which are characteristic of indole, since in the main the reactions are carried out with typical aromatic amines.

In the present work we started with 1-methylindole, which was prepared by the methylation of indole with dimethyl sulfate in liquid ammonia (yield 95%) [15]. Then the 1-methylindole was reduced to 1-methylindoline (I) (80%) by the action of zinc in hydrochloric acid. Like dimethyl-o-toluidine, 1-methylindoline is easily nitrated by a mixture of sulfuric and nitric acids to yield 6-nitro-1-methylindoline.
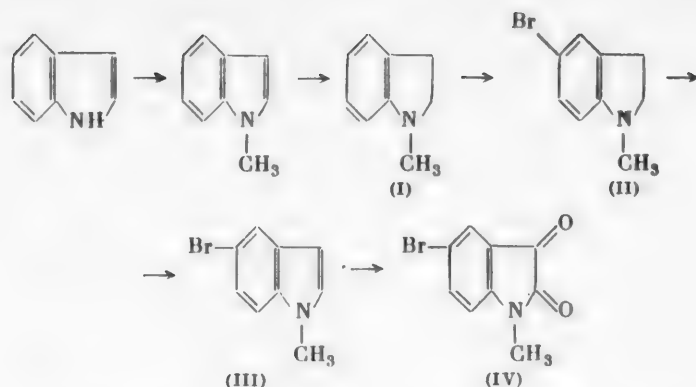
By the bromination of the sulfate of (I) in glacial acetic acid we obtained 5-bromo-1-methylindoline (II) in 66% yield. The latter, upon heating with chloranil in xylene, gave 5-bromo-1-methylindole (III) in 53% yield. Thus, the yield of (III) calculated on indole was 27%. It was not possible to use Raney nickel or palladium black to dehydrogenate 5-bromo-1-methylindoline, since in this instance splitting out of an atom of bromine occurred.

For proof of the structure of (III) we oxidized it with chromic acid. 5-Bromo-1-methylisatin (IV) was isolated. We also prepared 5-bromo-1-methylisatin by the method described in the literature (bromination of isatin and methylation of the 5-bromoisatin with dimethyl sulfate [16,17]). A mixed sample of (IV) obtained by the oxidation of (III), and (IV) obtained from isatin gave no depression in melting point.

1-Methylindoline (I) readily entered into an azo coupling reaction with sulfanilic acid. As is known, dimethyl-o-toluidine couples only in strongly alkaline media and moreover only with such active diazo compounds as dichlorodiazobenzene, [18, 19]. In contrast to this,(I) coupled in mineral acid medium,quantitatively forming the azo dye (V), which was extremely difficultly soluble in water.
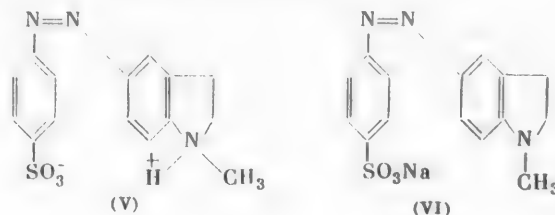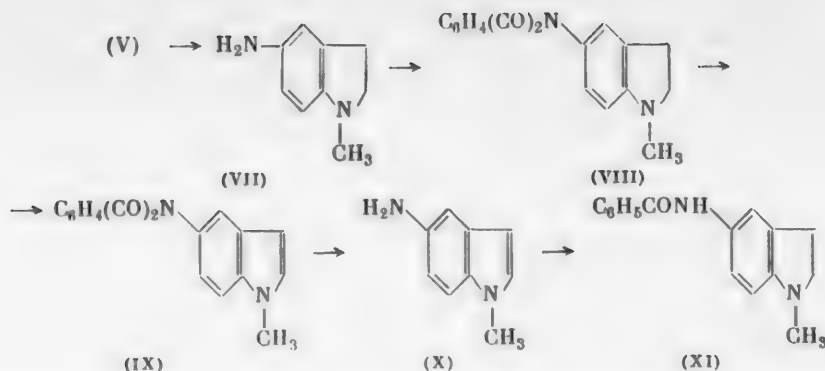

Apparently (V) was an inner salt. In this case, if azo coupling was carried out in alkaline medium,it was possible to separate the very water-soluble sodium salt of the azo compound (VI). The azo dye (V) dissolved in alkali upon heating the solution had the same color as a solution of (VI) in water. Upon acidification, the color changed. The absorption spectra in the ultraviolet region for (V) and (VI) were similar.

When (V) or (VI) was reduced with stannous chloride in hydrochloric acid (or with sodium hydrosulfite in weakly alkaline medium), we obtained 5-amino-1-methylindoline (VII) (59%) — a compound very similar in its properties to unsym-dimethyl-p-phenylenediamine.

Heating (VII) to 180° with phthalic anhydride gave a quantitative yield of 5-phthalimido-1-methylindoline (VIII). The latter was dehydrogenated with chloranil to 5-phthalimido-methylindole (IX) (49%).Upon boiling (IX) with hydrazine hydrate in methyl alcohol, we obtained 5-amino-1-methylindole (X) (80%).The yield calculated on the indole was 17.5%. In the free state (X) was a very unstable compound,which quickly resinified upon storage.

The compound showed very distinct triboluminescent properties. When the crystals were ground, a blue luminescence appeared, noticeable even in daylight. Upon simply shaking the crystals in a glass test tube in the dark, bright blue flashes were visible.

(V) → H_2N—[indole structure]—CH_3 (VII) → $C_6H_4(CO)_2N$—[indole structure]—CH_3 (VIII) →

→ $C_6H_4(CO)_2N$—[indole structure]—CH_3 (IX) → H_2N—[indole structure]—CH_3 (X) → C_6H_5CONH—[indole structure]—CH_3 (XI)

By benzoylation of (X) by the Schotten-Baumann method, 5-benzoylamido-1-methylindole (XI) was obtained.

To determine the position of the amino group in 5-amino-1-methylindoline (VIII), it was replaced with bromine by the Sandmeyer reaction. A mixed sample of the picrate of 5-bromo-1-methylindoline obtained by the bromination of 1-methylindoline and the picrate of 5-bromo-1-methylindoline obtained by diazotization of 5-amino-1-methylindoline gave no depression in melting point.

Dimethyl-o-toluidine is not nitrosated by nitrous acid under the conditions in which dimethylaniline usually is prepared. In an attempt to nitrosate the 1-methylindoline in such a manner, we were not able to isolate 5-nitroso-1-methylindoline. However, if without trying to isolate the nitroso derivative we introduced zinc dust into the reaction mixture, then 5-amino-1-methylindoline was formed in low yield (isolated as the benzoyl derivative). By nitrosation of 1-methylindoline with butyl nitrite (in the presence of hydrogen chloride) we succeeded in obtaining and isolating 5-nitroso-1-methylindoline (XII) in 37% yield.

To prove the structure of (XII), it was reduced and converted to the benzoyl derivative. 5-Benzoylamido-1-methylindoline obtained from (XII) and 5-benzoyl-amido-1-methylindoline obtained from (VII) gave no depression in a mixed melting point test.

We determined the molecular refraction for 5-bromo-1-methylindole (III). The value of MR_D found agrees with the calculated value, if the increment of the molecular refraction for nitrogen is taken as 4.360 (as in a quaternary aliphatic-aromatic amine). Since up to the present time there have been no reports in the literature of the measurement of MR_D for the indoles, we determined MR_D for 1-methylindole; the value found agreed with the calculated.

ON—[indole structure]—N—CH_3
(XII)
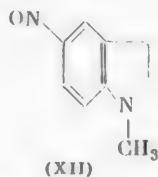
EXPERIMENTAL

1-Methylindole. 1-Methylindole prepared by methylating indole with dimethyl sulfate in liquid ammonia [15] had: b.p. 113° (5 mm), d_4^{20} 1.4076, n_D^{20} 1.5993, MR_D 42.80; calc. 42.95. •

Colorless liquid, quickly becoming yellow on storage. It did not have a characteristic indole or skatole odor.

5-Bromo-1-methylindoline (II). 39.9 g of (I) was dissolved in 100 ml of glacial acetic acid, 15.6 ml of conc. H_2SO_4 was added, and 48 g of bromine was run in dropwise with vigorous stirring. When addition of the bromine had been completed, the reaction mixture was sti rred for 1 hour more, and then the red solution was poured into an excess of alkali. The reaction product was steam-distilled. An ether extract was dried with potassium carbonate. Upon distillation, 41.3 g (66.3%) was obtained of a fraction with b.p. 114-120° at 2 mm. The almost colorless liquid darkened upon keeping in the air. The compound was distilled repeatedly.

B.p. 120° at 2 mm, d_4^{20} 1.4309, n_D^{20} 1.6082, MR_D 51.27; calc. 51.19.

•Here and in subsequent cases, in calculating MR_D, the increment for nitrogen was taken as 4.360.

Found % C 51.07; H 4.81. $C_9H_{10}NBr$. Calculated % C 50.97 H 4.75.

Oxalate of 5-bromo-1-methylindoline. M.p. 137-138° (with decomp., from anhydrous alcohol).

Found % N 4.26. $C_{11}H_{12}O_4NBr$. Calculated % N 4.63.

Picrate of 5-bromo-1-methylindoline. Yellow-greenish crystals. M.p. 151-152.5° (from alcohol).

Found % C 40.93; H 3.30; N 12.70. $C_{15}H_{13}O_7N_4Br$. Calculated %: C 40.83; H 2.97; N 12.70.

5-Bromo-1-methylindole (III). A solution of 19.9 g of (II) and 23 g of chloranil in xylene was boiled for an hour and a half. The dark reaction mixture was treated with alkali, filtered, and the xylene layer was washed successively with dilute alkali solution, water, hydrochloric acid (1:1) and water. (III) was distilled in vacuo. B.p. 136-140° at 2 mm. Yield 10.47 g (53%). The thick, slightly colored liquid turned yellow on keeping. The compound was distilled repeatedly.

B. p. 147-148° at 4 mm, d_4^{20} 1.4916, n_D^{20} 1.6392, MR_D 50.70; calc. 50.

Found %: C 51.46; H 4.09; N 6.43. C_9H_8NBr. Calculated %: C 51.45, H 3.84; N 6.67.

Picrate of 5-bromo-1-methylindole was prepared in benzene. Orange crystals. M.p. 88.5-89° (from benzene).

Found %: N 12.78. $C_{15}H_{11}O_7N_4Br$. Calculated %: N 12.75.

5-Bromo-1-methylisatin (IV). To a solution of 3.8 g of (III) in 20 ml of glacial acetic acid was added dropwise a solution of 2.5 g of CrO_3 in 25 ml of 80% acetic acid. Slight evolution of heat and formation of a precipitate were observed. In 2 hours the reaction mixture was poured into water (150 ml), filtered, and extracted with chloroform. After the chloroform was evaporated, 0.4 g of (IV) was obtained. M.p. 168.5-170°. A mixed sample with known 1-methyl-5-bromoisatin gave no depression in melting point.

Found %: N 5.85. $C_9H_6O_2NBr$. Calculated %: N 5.84.

5-(p-Sulfophenylazo)-1-methylindoline (V). A. To a solution of 13.3 g of (I) in 40 ml of HCl (1:1) was added a solution of diazotized sulfanilic acid (20.9 g), while the mixture was cooled below 0°. Then several milliliters of 30% NaOH were added, but the reaction medium was kept strongly acid. At a pH of 2, rapid formation of the azo dye started. The whole reaction mixture congealed as a dark-red mass. The compound was filtered off, washed with water, and dried in a drying oven at 150°; 32 g (quantitative yield) was obtained. The dark raspberry-colored compound was very poorly and slowly soluble in hot water. (It weakly colored the hot water, and precipitated from cold water as needles.) It decomposed upon heating above 300°.

Found %: C 56.71; H 4.83; N 13.19. $C_{15}H_{15}O_3N_3S$. Calculated %: C 56.76; H 4.76; N 13.25.

UV absorption spectrum: λ_{max} 262; $lg\epsilon_{max}$ 3.217; λ_{max} 428. $lg\epsilon_{max}$ 3.490. (Absorption spectrum measured with SF-4 spectrophotometer. The solvent was water).

B. Azo coupling was carried out as described in the preceding experiment, but excess alkali was added (until there was a strongly alkaline reaction). The reaction mixture was left for a day in the refrigerator. The crystals of (VI) that separated out were filtered off. The compound was dried in an oven at 150°. The yield was quantitative. The compound separated from the reaction mixture as the hydrate, which melted around 30° The desiccated compound (red-orange crystals) decomposed upon heating above 300°. After recrystallization from alcohol, crystals with a strong red luster were obtained.

Found %: C 52.82; H 4.26; N 12.41. $C_{15}H_{14}O_3N_3SNa$. Calculated %: C 53.08; H 4.16; N 12.38.

UV absorption spectrum: λ_{max} 266; $lg\epsilon_{max}$ 3.747; λ_{max} 430; $lg\epsilon_{max}$ 4.012.

5-Amino-1-methylindoline (VII). The azo dye (V), which was obtained from 13.3 g of indoline and 20.9 g of sulfanilic acid, was placed in 200 ml of conc. HCl and 100 g of $SnCl_2$ was added, after which the reaction mixture was heated to boiling for 1 hour. Alkali was added to the cooled mixture until the reaction was strongly alkaline, and the mixture was repeatedly extracted with ether. The extract was dried with potassium carbonate, the ether was distilled off, and (VII) was distilled in vacuo. B.p. 123.5° at 3 mm. M.p. 94-96° (with decomp., in a sealed capillary). The white crystalline material sublimed upon heating. It decomposed when kept.

Found %: C 72.94; H 8.24. $C_9H_{12}N_2$. Calculated %: C 72.93; H 8.16.

5-Benzoylamido-1-methylindoline was prepared by the benzoylation of (VII) by the Schotten-Baumann method. M.p. 176-176.5° (from alcohol). (It darkened when heated in a sealed capillary above 150°).

Found %: C 75.97; H 6.41. $C_{16}H_{16}ON_2$. Calculated %: C 76.16; H 6.39.

5-Phthalimido-1-methylindoline (VIII). The compound was prepared by heating equimolecular amounts of (VII) and phthalic anhydride to 180°. Yellow crystals. M.p. 172-173° (from alcohol).

Found %: C 73.30; H 5.18. $C_{17}H_{14}O_2N_2$. Calculated %: C 73.36; H 5.07.

5-Phthalimido-1-methylindole (IX). 17 g of (VIII) and 14.2 g of chloranil were boiled in xylene for 4 hours. The xylene solution was treated with alkali, filtered, again washed with alkali, then with water, HCl (1:1), and water. The xylene solution was evaporated and 8.3 g (49%) of 5-phthalimido-1-methylindole was obtained. M.p. 211-212° (from xylene, then from benzine).

Found %: N 9.85. $C_{17}H_{12}O_2N_2$. Calculated %: N 10.14.

5-Amino-1-methylindole (X). To a mixture of 12.9 g of (IX) and 200 ml of alcohol was added 3 ml of hydrazine hydrate. The mixture was heated to boiling for 3 hours, the phthalazine that separated out was filtered off, the alcohol was evaporated in vacuo to half its volume, the residual solution was poured into water, alkali was added, and (X) was extracted with ether. The ether extract was dried with potassium carbonate, the ether was distilled off, and 6 g (93%) of 5-amino-1-methylindole was obtained by distilling in vacuo. White crystals. B.p. 143-144° at 2 mm. M.p. 100-101.5° (in a sealed capillary). It sublimed upon heating. It decomposed when kept. Strong blue triboluminescence.

Found %: C 73.87; H 7.12. $C_9H_{10}N_2$. Calculated %: C 73.93; H 6.89.

5-Benzoylamido-1-methylindole (XI) was prepared by benzoylation by the Schotten-Baumann method. M.p. 191-192° (in a sealed capillary) (from aqueous alcohol, then from toluene).

Found %: N 10.79. $C_{16}H_{14}ON_2$. Calculated %: N 11.20.

5-Bromo-1-methylindoline (II) from 5-amino-1-methylindoline (VII). A solution of 1.44 g of $NaNO_2$ in water was added to 50 ml of hydrobromic acid (1:1) with vigorous cooling (below 0°) and stirring. To the mixture of nitrous and hydrobromic acids obtained was added a solution of 2.96 g of (VII) in 30 ml of HBr (1:1). The resulting mixture was added drop by drop to a boiling suspension of freshly prepared Cu_2Br_2 in 50 ml of HBr (1:1). After completion of the adddition of the diazo solution, the mixture was heated for 3 hours more, then cooled, made strongly alkaline, the (II) was steam-distilled off and extracted with ether, and an ether solution of picric acid was added to the ether solution of (II). The picrate of 5-bromo-1-methylindoline was obtained. M.p. 147-148°. A mixed sample with known 5-bromo-1-methylindoline gave no depression in melting point.

5-Nitroso-1-methylindoline (XII). 13.3 g of (I) was dissolved in 50 ml of dry ether, 10.3 g of butyl nitrite was added, and a current of dry HCl was passed through, while the mixture was stirred and cooled with water. In 20 minutes the precipitate of indoline hydrochloride that had separated out was filtered off, washed with dry ether, dissolved in water, and aqueous ammonia solution was added. The nitroso derivative precipitated as a black mass, which partially crystallized. The crystals of (XII) were removed. the mother liquor was extracted with chloroform, and the chloroform was evaporated. The nitroso derivative obtained was pressed out on a porous plate. 6 g of brown-green crystals (37%) were obtained. Solutions in benzine had an emerald-green color. Upon crystallization from benzine, green crystals separated out, which then turned red-brown. M.p. 84.5-85.5° (from benzine).

Found %: C 66.50; H 6.36. $C_9H_{10}ON_2$. Calculated %: C 66.64; H 6.21.

UV absorption spectrum. Solvent water; λ_{max} 283; $\lg \epsilon_{max}$ 3.404; λ_{max} 425; $\lg \epsilon_{max}$ 4.269.

Solvent dilute hydrochloric acid; λ_{max} 246; $\lg \epsilon_{max}$ 3.480; λ_{max} 345; $\lg \epsilon_{max}$ 4.252.

SUMMARY

1. A method of synthesis has been proposed for indoles substituted in the benzene ring by the method of "temporary shutting off" of the pyrrole nucleus of the indole; the indole is converted to the indoline, the sub-stitutent is introduced into the benzene ring of the indoline, and the substituted indoline obtained is dehydrogenated to form the corresponding indole.

2. The preparation of 5-amino-1-methylindole and 5-bromo-1-methylindole has been described.

3. 5-Bromo-, 5-amino-, 5-nitroso, and 5-(p-sulfophenylazo)-1-methylindolines have been prepared.

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CONFIGURATION AND PROPERTIES OF UNSATURATED ACIDS AND THEIR DERIVATIVES.

X. THIOCYANATION OF OLEIC AND ELAIDIC ACIDS AND THEIR ESTERS

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It has been shown previously that oleic and elaidic acids and also their methyl esters react at different rates with thiocyanogen solutions; oleic acid and methyl oleate are thiocyanated considerably more rapidly than elaidic acid and methyl elaidate [1]. In view of the fact that the different effect of alcohol radicals on the reactivity of cis- and trans-derivatives of unsaturated acids has been established in earlier investigations [2], it seemed to us necessary to inquire into this problem in the instance of the thiocyanation reaction. Moreover, thiocyanation and thiocyanate compounds have recently attracted the attention of chemists also because they have various practical uses in the vulcanization of rubber, in medicine [3], in the dye industry [4], insecticide industry [5], etc.

In order to study the thiocyanation reaction, we synthesized the methyl, ethyl, butyl, isobutyl, tert-amyl, n-hexyl, benzyl, phenyl, and α-naphthyl esters of oleic and elaidic acids and set up experiments on their thiocyanation at different temperatures and different concentrations of the reagents. Below are presented some of the most essential results of our experiments, which, as in our earlier work on the hydrogenation, oxidation, halogenation, and saponification of the geometrically isomeric esters of unsaturated acids, indicate that the cis-form is thiocyanated more rapidly than the trans-form .Moreover, in thiocyanation the effect of the length of the chain and the volume of the alcohol radical is revealed especially clearly.

In order to clarify the chemical affinities in the thiocyanation reaction, we isolated and characterized the end products of the thiocyanation of the methyl esters of oleic and elaidic acids — methyl dithiocyanooleate and methyl dithiocyanoelaidate.

In comparing the data obtained by us on thiocyanation with the results of hydrogenation, oxidation, and halogenation, attention is attracted by the similarity of the numerical data on hydrogenation and thiocyanation, which cannot be said of the oxidation and halogenation reactions. To more fully elucidate this problem, we set up special experiments on the hydrogenation of a series of esters for which information is lacking in the literature.

EXPERIMENTAL

Preparation of starting materials. The oleic acid necessary for the investigation was prepared from commercial oleic acid by purification according to Twitchall's method [6] and recrystallization of its lithium salt [7]. Elaidic acid was prepared by the isomerization of oleic acid with metallic selenium [8]. Preparation of the methyl, ethyl, n-butyl, isobutyl, and benzyl esters was carried out by the usual method — heating the acid and the appropriate alcohol on a water bath in the presence of sulfuric acid.

n-Hexyl oleate has not been described in the literature. We prepared it by direct esterification in the presence of sulfuric acid, and also from n-hexyl bromide and potassium oleate in anhydrous alcohol after 6 hours' heating on a boiling water bath. After vacuum distillation in a current of CO_2, the n-hexyl oleate was obtained as a colorless oily liquid without odor. It was soluble in ethyl ether, alcohol, benzene, $CHCl_3$, and glacial acetic acid.

TABLE 1

Constants of Esters of Oleic and Elaidic Acids

Esters	Temperature Boiling (pressure in mm)	Temperature Melting	d_t^x	n_D^{20}	Acid number	Molecular refraction Found	Molecular refraction Calculated	Iodine number (Gyublyu)** Found	Iodine number (Gyublyu)** Calculated	Saponification number Found	Saponification number Calculated
n-Hexyl oleate	206—208°(5)	—	0.8688	1.4566	0.00	114.71	114.22	69.01	69.23	153.72	153.04
n-Hexyl elaidate	216—217(5)	—	0.8672	1.4545	0.00	114.38		69.12		152.91	
ter-Amyl elaidate	207—208(5)	—	0.8662	1.4522	0.00	109.83	109.60	72.21	72.03	159.01	159.20
Phenyl oleate	230—232(1)	—	0.9281	1.485ᵥ	0.00	110.80	110.62	71.02	70.94	156.8	156.4
Phenyl elaidate	242—243(5)*	30.5°	0.9383*	1.4810*	0.00	110.48		70.29		155.9	
α-Naphthyl oleate	290—292(5)	—	0.9792	1.5085	0.00	124.32	124.22	61.90	62.12	137.7	137.5
α-Naphthyl elaidate	302—302.5(5)	35.5	0.9804*	1.5058*	0.00	123.84		62.10		136.9	

*At 40°.
**Transliteration of Russian. Probably Hübl-Waller reagent

TABLE 2

Amount of Thiocyanogen (in %) Added at 15° and 0.01 N Concentrations of Each Reagent in Glacial Acetic Acid

Time from start of experiment (in minutes)	Acids oleic	Acids elaidic	methyl oleate	methyl elaidate	ethyl oleate	ethyl elaidate	n-butyl oleate	n-butyl elaidate	isobutyl oleate	isobutyl elaidate	tert-amyl oleate	tert-amyl elaidate	n-hexyl oleate	n-hexyl elaidate	phenyl oleate	phenyl elaidate	benzyl oleate	benzyl elaidate	α-naphthyl oleate	α-naphthyl elaidate
240	41.9	25.7	66.9	45.5	61.9	41	58.1	37.8	56.2	35.5	53.5	32.5	50.5	30.2	47.4	28.6	46.4	27.5	43.5	26.5
360	50.5	36.0	75.0	56.9	70.8	52.1	65.6	49.0	64.5	47.5	61.5	44.5	58.3	43.3	56.1	41.6	54.9	39.7	52.5	38.6
Average rate constant from equation for bi-molecular reaction $K_t \cdot 10^5$	2.8	1.7	7.8	3.6	6.2	3.0	5.4	2.7	5.0	2.5	4.3	2.2	4.0	2.0	3.3	2.0	3.2	1.8	3.0	1.7

•The course of the reaction in each experiment was observed by 20 determinations of the thiocyanogen number.

TABLE 3

Amount of Thiocyanogen (in %) Added at 25° and 0.01 N Concentration of Each Reagent in Glacial Acetic Acid

Time in minutes from start of experiment*	Acids		Esters							
	Oleic	Elaidic	Methyl oleate	Methyl elaidate	Ethyl oleate	Ethyl elaidate	n-Butyl oleate	n-Butyl elaidate	Isobutyl oleate	Isobutyl elaidate
60	27.2	20.0	68.0	32.8	62.9	31.0	56.7	30.0	53.2	29.0
840	82.5	76.1	95.6	84.9	94.3	84.3	93.9	84.0	92.7	83.4
Average rate constant from equation for bi-molecular reaction $K_r \cdot 10^5$	5.9	3.8	22.7	7.0	18.7	6.6	17.5	6.3	15.2	6.1
Activation energy (cals/mole)	12.7	13.8	18.3	10.4	18.9	12.9	19.8	14	18.7	15.3
Reaction constant	$1.2 \cdot 10^5$	$5.2 \cdot 10^5$	$5.3 \cdot 10^9$	$1.6 \cdot 10^4$	$1.2 \cdot 10^{10}$	$1.8 \cdot 10^5$	$9.1 \cdot 10^{10}$	$1 \cdot 10^6$	$7.1 \cdot 10^9$	$9.2 \cdot 10^6$

II continuation

Time in minutes from start of experiment*	Esters									
	tert-Amyl oleate	tert-Amyl elaidate	n-Hexyl oleate	n-Hexyl elaidate	Phenyl oleate	Phenyl elaidate	Benzyl oleate	Benzyl elaidate	α-Naphthyl oleate	α-Naphthyl elaidate
60	50.0	27.5	46.6	27.3	45.6	25.9	39.5	24.5	35.1	23.4
840	90.0	81.4	89.1	80.7	88.6	79.8	87.6	79.0	86.6	78.4
Average rate constant from equation for bi-molecular reaction $K_r \cdot 10^5$	11.4	5.2	10	4.9	9.5	2.8	8.6	4.5	8.2	4.3
Activation energy (cals/mole)	16.7	14.8	15.7	15.7	18.6	15	17.3	15	17.3	15.2
Reaction constant	$1.8 \cdot 10^8$	$3.3 \cdot 10^6$	$2.9 \cdot 10^7$	$1.3 \cdot 10^7$	$3.8 \cdot 10^9$	$4.5 \cdot 10^6$	$2.6 \cdot 10^8$	$4 \cdot 10^6$	$3.9 \cdot 10^8$	$5.5 \cdot 10^6$

*For each experiment 18 determinations of the thiocyanogen number were carried out.

n-Hexyl elaidate has not been described in the literature. We prepared it by direct esterification in the presence of H_2SO_4 in 69% yield as an oily liquid without odor. It was soluble in the usual organic solvents.

tert-Amyl oleate was prepared in absolute ether medium from $C_5H_{11}MgBr$ and oleic acid chloride by heating for 2 hours on a water bath and subsequently holding the reaction mixture for 12 hours. After the reaction was over, the ether solution was poured off from the precipitate and the latter was mixed with a small amount of ice and dissolved in 10% acetic acid. The solution obtained was treated with ether and the ethereal extracts were added to the previously decanted ether solution. The ether solution was neutralized with 0.5 N alcoholic KOH, washed with water until the reaction was neutral, dried with sodium sulfate, and distilled. The high-boiling fraction was redistilled in vacuo in a current of CO_2. The pure ester, obtained in a yield of about 50%, was an oily, colorless liquid.

tert-Amyl elaidate has not been described in the literature. We prepared it in the same way as the amyl oleate, with a yield of 50%, as a colorless liquid without odor, soluble in the usual solvents.

Phenyl oleate was prepared from oleic acid chloride and potassium phenolate in 52% yield. In the literature phenyl oleate has been characterized only by its boiling point.

TABLE 4

Amount of Hydrogen (in %) Adding to Esters of Oleic and Elaidic Acids on Pd-Catalyst at 22° for 60 minutes

Ester	Amount of hydrogen (in %)	Ester	Amount of hydrogen (in %)
Butyl oleate	90	Benzyl oleate	70
Butyl elaidate	79	Benzyl elaidate	54
Isobutyl oleate	86	Phenyl oleate	72
Isobutyl elaidate	75	Phenyl elaidate	63
Hexyl oleate	78	α-Naphthyl oleate	63
Hexyl elaidate	61	α-Naphthyl elaidate	52
tert-Amyl oleate	75		
tert-Amyl elaidate	65		

Phenyl elaidate was prepared by us for the first time from phenol and elaidic acid chloride in pyridine solution in 46% yield. Phenyl elaidate was a solid, colorless material with a phenol odor, which dissolved in ether, alcohol, benzene, carbon tetrachloride, and glacial acetic acid.

α-Naphthyl oleate was prepared by us for the first time from potassium α-naphtholate and oleic acid chloride [9]. The yield of pure ester was about 48%. α-Naphthyl oleate at room temperature was a yellowish liquid with a slight odor. It dissolved in the usual solvents. Upon cooling with ice it solidified to a yellowish crystalline mass.

α-Naphthyl elaidate was prepared by us for the first time by esterification in the presence of pyridine [9] in 45% yield. It was a solid yellowish crystalline material with a slight naphthol odor. It dissolved in organic solvents.

Constants characterizing their degree of purity were determined for the esters that were prepared by us for the first time, and also for phenyl oleate (Table 1).

Experiments on the thiocyanation of esters of oleic and elaidic acids. The results of the thiocyanation experiments carried out at different temperatures, the rate constants of the reaction, the activation energies, and the reaction constants presented in Tables 2 and 3 indicate the significant role of the steric factor in these reactions.

The difference in the reactivity of the cis- and trans- forms attracts attention. In thiocyanation the length of the carbon chain of the alcohol radical and its volume also have an effect. The greatest effect in this connection is exerted by the naphthyl radical.

Preparation of the dithiocyanates of the methyl esters of oleic and elaidic acids. In a flask with a well ground stopper was placed a weighed sample (10 g) of the methyl ester of oleic or elaidic acid, and over the sample was poured 10 ml of thiocyanogen solution prepared from 100 g of Pb(CNS)$_2$ in 225 ml of 98% acetic acid with 10% acetic anhydride and 10 ml of dry bromine. The mixture was left for 24 hours in the dark at room temperature. Then the mixture was poured into a separatory funnel and the thiocyanate obtained was separated from the polymer by extraction with ether. The ether solution was washed several times with distilled water, neutralized with 0.1N alcoholic solution of KOH, and washed with water to a neutral reaction; the ether solution was dried with anhydrous sodium sulfate and the ether was distilled off

The thiocyanates, which were obtained in almost 100% yield, were yellowish oily liquids with a specific odor, insoluble in water, readily soluble in alcohol, ether, benzene, chloroform, CCl$_4$, and glacial acetic acid. It was not possible to convert the compounds obtained to the solid state. When an attempt was made to distil them in vacuo, the thiocyanates decomposed with the formation of tarry products of unpleasant odor.

Methyl Dithiocyanooleate

d_4^{20} 1.0091, $n^{20}D$ 1.4970.

Found %: N (by the Kjeldahl method) 6.49; S (by the Messinger method) 15.30; CNS (by the method of Panchenko and Smirnov) 28.00. C$_{19}$H$_{36}$O$_2$(CNS)$_2$. Calculated %: N 6.78; S 15.50; CNS 28.16.

Methyl dithiocyanoelaidate.

d_4^{20} 1.1040, n_D^{20} 1.4946

Found %: N (by the Kjeldahl method) 6.52; S (by the Messinger method) 15.25; CNS (by the method of Panchenko and Smirnov) 27.93. C$_{19}$H$_{36}$O$_2$(CNS)$_2$. Calculated %: N 6.78; S 15.50; CNS 28.16.

Experiments on the hydrogenation of the esters of oleic and elaidic acids. The hydrogenation conditions were similar to those described previously [1]. Mixing of the Pd/BaSO$_4$ catalyst was carried out with the aid of a magnetic stirrer. The results of the hydrogenation are presented in Table 4.

SUMMARY

1. The following compounds, which have not been described in the literature, were prepared and their properties described: n-hexyl oleate, n-hexyl elaidate, tert-amyl elaidate, α-naphthyl oleate, α-naphthyl elaidate, phenyl elaidate, methyl dithiocyanooleate, and methyl dithiocyanoelaidate.

2. It has been established that oleic acid and the oleates are thiocyanated considerably more rapidly than elaidic acid and the elaidates; in addition, the length of the chain of the alcohol radical and its volume have a greater effect in the oleates than in the elaidates.

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STEROIDS

II. SYNTHESIS OF PROGESTERONE FROM SOLASODINE.

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We have reported previously the development of a convenient method for preparing the valuable medicinal compound cortisone acetate from solasodine through progesterone, 11α-hydroxyprogesterone, and 21-bromo-pregnanol-17α-trione-3, 11, 20 [1].   In the present experimental article data are presented relative to the conversion of solasodine to the hormone of the corpus luteum, progesterone.

Solasodine (I) is an aglucone of steroidal glucoalkaloids isolated from "bird nightshade" (Solanum aviculare Forst.).   This plant was introduced into culture in our country in VILAR* by P. N. Kibal'chich and I. N. Gerasimenko.   The preparation of solasodine has been accomplished by A. S. Labenskii in our institute.

The synthesis of progesterone from solasodine has not been described in the literature.   There exists only a brief indication by Sato, Miller and Mosettig [2] that when solasodine is heated with acetic anhydride with subsequent oxidation of the reaction product by chromic acid and saponification by a methanol solution of potassium hydroxide, a semicrystalline product is formed.   The latter was chromatographed, acetylated, and the acetate that was obtained was again subjected twice to chromatographing, as a result of which the acetate of $\Delta^{5,16}$ -pregnadienol-3β -one-20 and 3β -acetoxy-16-methoxy-20-keto-Δ^{5}'-pregnene were isolated along with other unidentified products.   Neither the experimental conditions nor the yield of the acetate of $\Delta^{5,16}$-pregnadien-ol-3β -one-20 (judged on the whole, it was insignificant) was stated.* We have established that the process of converting solasodine to the acetate of $\Delta^{5,16}$-pregnadienol-3β -one-20 (IV) can be carried out in three stages, without isolation of the intermediate products: a) acetylation of the hydroxyl group in the 3-position and opening of the six-membered nitrogen-containing ring; b) oxidative cleavage of the double bond with formation of a keto group in position 20; c) splitting off of the side chain from position 16 with the formation of a $\Delta^{16(17)}$-double bond.   It should be pointed out that the exact mechanism of these reactions has not yet been established by us and this will be the object of further investigation.

It must be noted that in spite of the structural and configurational similarity of solasodine and diosgenin, the behavior of   these compounds in the reaction under consideration is completely different. While, according to the data of Wall et al. [3], heating the acetate of diosgenin with acetic anhydride at 195° for 18 hours leads to the formation of $\Delta^{5,16}$-pregnadienol-3β -one-20 in 78% yield, in the case of solasodine complete resinification is observed under these conditions. We have found that opening of the nitrogen-containing heterocyclic ring (I) → (II) should be carried out in the presence of acid catalysts (p-toluenesulfonic acid gives the best results) in acetic acid medium using a minimum amount of acetic anhydride.

Oxidative cleavage of the double bond (II) → (III) can be carried out under various conditions. However, it is most expedient to carry out the oxidation with sodium bichromate in acetic acid at room temperature.

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* *After the article went to press, a report appeared by Sato, Latham, and Mosettig [13] which indicated that total yield of pregnane derivatives under these conditions was only 10% of theoretical.
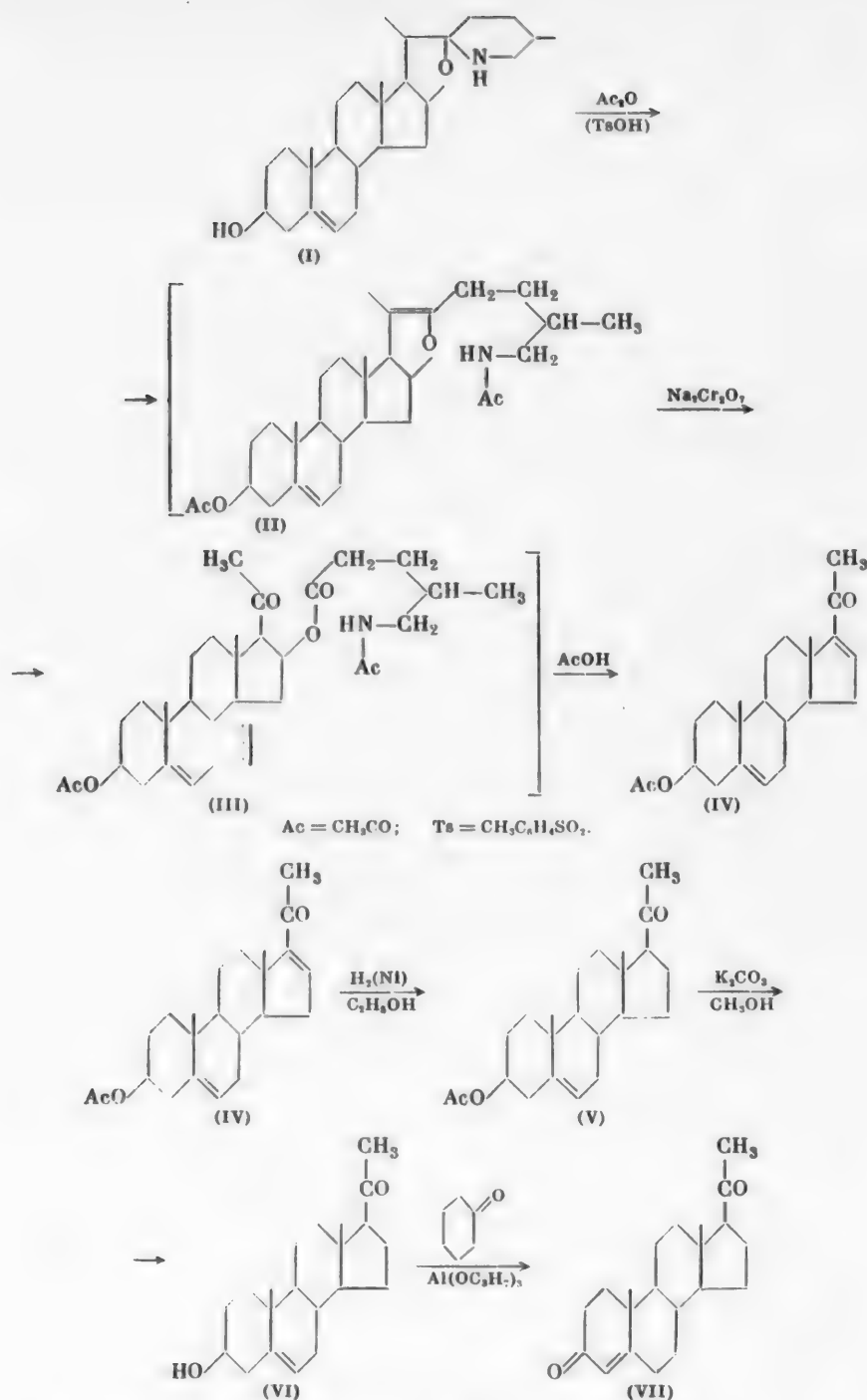
Splitting off of the side chain with the formation of a $\Delta^{16(17)}$-double bond (III) → (IV) can be carried out in both alkaline and acid media. In the first instance we used a solution of potassium hydroxide in tert-butyl alcohol (primary alcohols give 16-alkoxy derivatives here). Although this method gives good results, it requires the introduction of an additional step — acetylation with acetic anhydride in pyridine. Acid cleavage, similar to the work of Cameron et al. with a series of sapogenins [4], can be carried out by simply boiling the reaction mixture. In this case the conversion of solasodine to the acetate of $\Delta^{5,16}$-pregnadienol-3β-one-20 is accomplished

very compactly. The yield of acetate of $\Delta^{5,16}$-pregnadienol-3β-one-20 (IV) was 44% calculated on sola-sodine (I).

Thus, we succeeded in developing a convenient method for the preparation of the acetate of $\Delta^{5,16}$-pregna-dienol-3β-one-20 [5]. It should be pointed out that this compound is the key to the synthesis not only of pro-gesterone and cortisone, but also of other steroidal hormones: sex hormones [6], desoxycorticosterone [7], Reichstein's compound "S" [8], etc.

The further conversion of the acetate of $\Delta^{5,16}$-pregnadienol-3β-one-20 to progesterone was carried out according to the scheme proposed by Butenandt and Schmidt-Thomé [9] and Oppenauer [10].

The present method makes possible the preparation of progesterone (VII) from solasodine (I) in four stages in 33% yield.

EXPERIMENTAL

Acetate of $\Delta^{5,16}$-pregnadienol-3β-one-20 (IV). To a solution of 100 g of solasodine (containing 4.2% moisture) in 600 ml of 99.4% acetic acid was added a solution of 7.2 g of p-toluenesulfonic acid monohydrate in a mixture of 60 ml of the same acetic acid and 108 ml of acetic anhydride. The reaction mixture was stirred at room temperature for 1 hour and then boiled for 6 hours. It was cooled to 15-18°, 700 ml of 99.4% acetic acid was added, and a solution of 50 g of sodium bichromate in 300 ml of the previously mentioned acetic acid was added over a period of 20-30 minutes while the mixture was stirred and the temperature was kept at 15-22°. The reaction mixture was allowed to stand at the same temperature for 1 hour, 30 g of anhydrous sodium sulfate was added, the mixture was heated to 80°, 100 ml of acetic anhydride was added, and the mixture was boiled for 3 hours. Then 1300 ml of acetic acid was distilled off in vacuo (40-50 mm) at a bath temperature of 60-70°, the residue was cooled to 23-25°, and to it was added 570 ml of water over a period of 20-30 minutes with vigorous stirring. In 1 hour the precipitate of the acetate of $\Delta^{5,16}$-pregnadienol-3β-one-20 (IV) was separated by suction and washed on the filter with 55% (by volume) of acetic acid until the filtrate was colorless, then with water until there was no longer an acid reaction to litmus; 70.2 g of crude precipitate was recrystallized from 350 ml of alcohol. The yield of (IV), taking into account that obtained from the mother liquor, was 36 g (44%). M.p. 172-173°, $[\alpha]^{20}_D - 36°$ (c 0.9, CHCl$_3$). λ_{max} 238 mμ (lgϵ 4.0). The compound obtained did not give a depression in melting point when mixed with a known sample of the acetate of $\Delta^{5,16}$-pregnadienol-3β-one-20.

From the acetic acid mother liquor we isolated, by distilling off the acetic acid in vacuo and extracting with methylene chloride, about 9g of a material with m.p. 197-200°, the structure of which is being studied.

The acetate of Δ^5-pregnenol-3β-one-20 (V) was obtained by hydrogenation of (IV) over the skeletal nickel catalyst of A. K. Ruzhentseva, V. V. Kolpakova, and N. S. Goryacheva [11] in ethyl alcohol at room temperature and atmospheric pressure. Yield 90%. M.p. 146-148°.

Saponification of (V) to Δ^5-pregnenol-3β-one-20 (VI) was carried out by the method of O. S. Madaeva [12] with a methanolic solution of potassium carbonate. Yield of (VI) 95.5%. M.p. 188-190°, $[\alpha]^{20}_D + 23.9°$ (c 3, CHCl$_3$).

Progesterone or Δ^4-pregnenedione-3,20 (VII) was obtained by oxidation of (VI) according to Oppenauer's method with cyclohexanone in toluene in the presence of aluminum isopropylate. Yield 87%. M.p. 128-129°, $[\alpha]^{20}_D + 195°$ (c 0.5, alcohol). The compound obtained showed no lowering of the melting point when mixed with a known sample of progesterone and met the requirements of the State Pharmacopeia of the USSR.

SUMMARY

The synthesis of progesterone from solasodine has been accomplished.

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SYNTHESES BASED ON SCLAREOL.

I. INVESTIGATION OF THE REACTION PRODUCTS OF SCLAREOL AND HYDROGEN CHLORIDE

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The crystalline diterpene alcohol sclareol has attracted the attention of chemists by its unique structure (I) and availability. It is contained in muscatel sage [Salvia sclarea] and can be obtained easily as a by-product in the manufacture of the sage essential oil. The interest in sclareol that has appeared in recent years was elicited mainly by its structural relationship with ambrein [1], which is responsible for the perfume qualities of ambergris [2]. By oxidative decomposition of sclareol, it has actually been possible to prepare several pleasant-smelling compounds, which have been recommended as complete substitutes for the amber [3].

The possibilities of converting sclareol to new compounds of practical value are still far from exhausted; therefore we aimed to carry out a series of syntheses based on it. Expecting to obtain in the final accounting derivatives containing an amine group, we investigated the hydrochlorination of sclareol. However, we did not succeed in isolating the trichlorosclareol described in the literature [4,5], although we made repeated attempts. Instead of it, we obtained each time a liquid product of the composition $C_{20}H_{35}Cl$, which contained two double bonds. When we hydrogenated this product with palladium catalyst, 3 g-moles of hydrogen were absorbed and 1 g-mole of chlorine was quantitatively split out.

Analysis of the IR spectrum of this compound showed that in the region 850-1050 cm^{-1} it is close to the spectra of the sclarenes (II) and (III) obtained by dehydration of sclareol [6].

The absorption maxima in the region 888 and 908 cm^{-1} (Fig. 1) indicate that in the molecule of the reaction product of sclareol and hydrogen chloride there are tertiary-primary $>C=CH_2$ and secondary-primary $-CH=CH_2$ carbon-carbon double bonds.

In the spectrum of sclareol the frequencies 920 and 996 cm^{-1} correspond to the vinyl bond, as can be seen from a comparison of the absorption curves of sclareol and its hydrogenation product, dihydrosclareol (Fig. 2). Such a movement of the absorption maximum of the vinyl group toward the short-wave direction (from 908 to 920 cm^{-1}) in the sclareol spectrum is a result, apparently of the effect of the two hydroxyls.

The presence of a tertiary-primary carbon-carbon bond in the reaction product of sclareol and hydrogen chloride is also substantiated by the Raman spectra, in which a line at 1651 cm^{-1} is found. Moreover, in these spectra a line is found at 710 cm^{-1}, which indicates the presence of chlorine in the compound in question.

By careful oxidation of the monochloro derivative with potassium permanganate, two compounds were obtained. One of them, a neutral compound with the composition $C_{20}H_{32}O$ and m.p. 97-98°, did not contain an active hydrogen and did not give an oxime or semicarbazone. 1 g-mole of this compound absorbed 2 g-moles of hydrogen. No maximum characteristic of the carbonyl group was found in its IR spectrum (Fig. 3); the frequency 1075 cm^{-1}, according to the data in [7], corresponds to the oxide group $>C-O-C<$; the distinct maximum at 1010 cm^{-1}, apparently, also is characteristic of this group. Moreover, in the spectrum of this compound the band at 912 cm^{-1} is preserved, which is characteristic of the $-CH=CH_2$ group.

On the basis of these data it can be considered that the neutral compound is an oxide of structure (V).

The second compound, with m.p. 99-101°, was a hydroxy acid of the composition $C_{15}H_{26}O_3$, which should be assigned the formula (IV) on the basis of the results of chemical analysis and spectroscopic data.
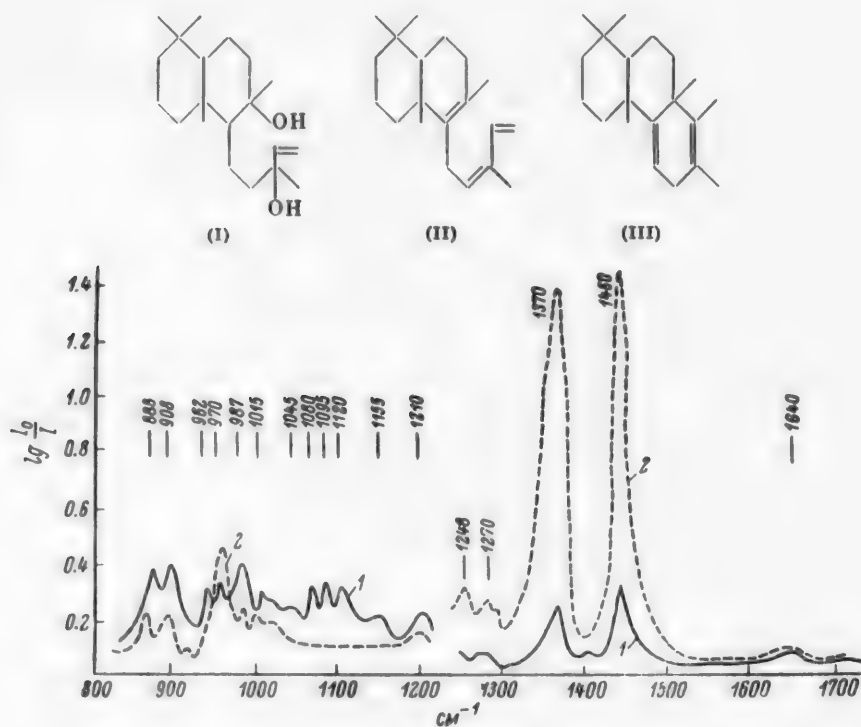
Fig. 1. Infrared-absorption spectra: 1) chloro derivative; 2) sclarene.
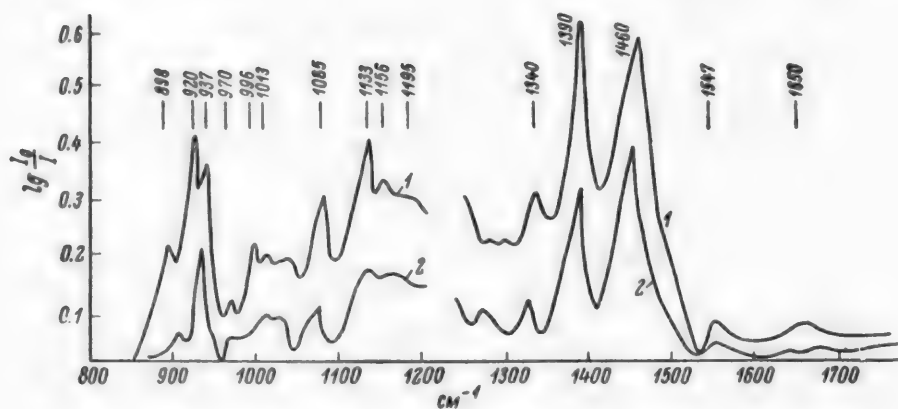
Fig. 2. Infrared-absorption spectra: 1) sclareol; 2) dihydrosclareol.
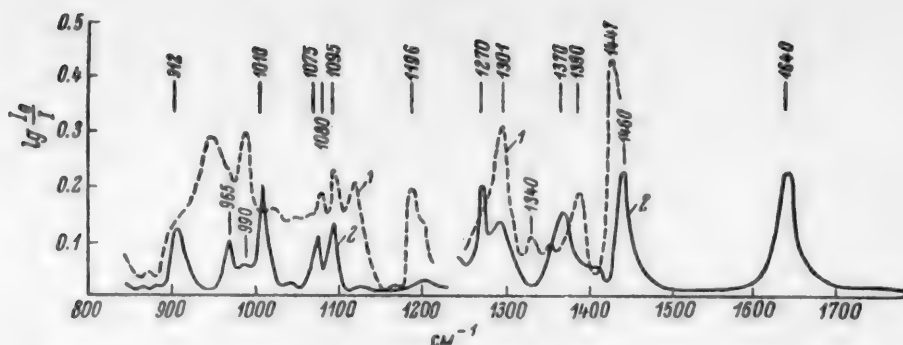
Fig. 3. Infrared absorption spectra: 1) hydroxy acid; 2) oxide.

The IR spectrum of the acid with maxima at 954, 1301, and 1447 cm^{-1} confirmed the presence of a carboxyl group, and the maxima at 1080 and 1340 cm^{-1} showed the presence of a hydroxyl group (Fig. 3). In the spectrum of sclareol the hydroxyl group corresponds to the maximum at 1085 cm^{-1} (Fig. 2), which differs little from the frequency 1089 cm^{-1} which, according to the data in [7], is characteristic of the tertiary hydroxyl in compounds of the sclareol series. The maximum at 1340 cm^{-1} was found in the spectrum of sclareol too, where, as can be seen from comparison with the spectrum of sclarene (Fig. 1), it also corresponded to the hydroxyl group. The strong maxima at 1390 and 1460 cm^{-1} present in both spectra are characteristic of methyl groups   C-CH$_3$ and therefore do not require special consideration.

The acid (IV) was also obtained by oxidation of the oxide (V); consequently the oxide must be considered an intermediate oxidation product. In turn, the structure of the oxide (V) can be explained only by assuming the formation, in the first stage of the oxidation, of the chloroglycol (VI), which could be produced by the oxidation of the chloro derivative (VII) under mild conditions.
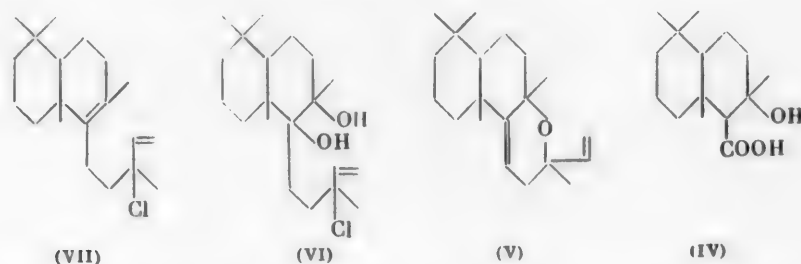
All these data indicate that the reaction product of sclareol and hydrogen chloride is a mixture of isomers of the composition C$_{20}$H$_{33}$Cl   one of which is compound (VII).

EXPERIMENTAL

Reaction of sclareol and hydrogen chloride   30 g of sclareol was dissolved in 150 ml of absolute ether and a stream of dry hydrogen chloride was passed for 5 hours through the solution, which was cooled to 0°. The solution saturated with hydrogen chloride was allowed to stand for 24 hours at room temperature. Then the ethereal solution was washed with ice water, 10% sodium carbonate solution, and again with water until the chloride ions were completely removed. The ethereal solution was dried with sodium sulfate and then the ether was distilled off on a water bath. The residue was distilled in vacuo. 24.3 g of a colorless, viscous liquid was obtained.

B.p. 158-162° at 1 mm, d$_4^{20}$ 1.0054, n$_D^{20}$ 1.5222, MR$_D$ 93.89; calc. 94.09.

Found %: Cl 11.32. C$_{20}$H$_{33}$Cl$_{F2}$. Calculated % Cl 11.50.

Upon catalytic hydrogenation, the amount of hydrogen absorbed was 1.87% (based on the molecular weight of the compound). The hydrogen calculated for 2 double bonds and 1 atom of chlorine was 1.95.

<u>Oxidation of the product of hydrochlorination.</u> 24 g of the compound was dissolved in 150 ml of acetone, and a solution of 57 g of potassium permanganate in 3 liters of acetone was added in small portions with cooling. After the color of the permanganate did not disappear in 5 hours, the manganese dioxide was removed. After the acetone was distilled off, the reaction product was dissolved in 150 ml of ether, washed with 10% sodium carbonate solution, and then the ether was distilled off. The residue was a thick, yellow, pleasant-smelling liquid, which solidified upon standing. After recrystallization from acetone, 2.1 g of a white, crystalline compound was obtained with m.p. 97-98°.

Found %: C 83.01; H 11.40; H (active) 0.03. M (cryoscopic) 283.3. $C_{20}H_{32}O$. Calculated %: C 83.33; H 11.11; H (active). M 288.

Upon catalytic hydrogenation, the amount of hydrogen absorbed was 1.49% (based on the molecular weight of the compound). The hydrogen calculated for 2 double bonds was 1.40.

The manganese dioxide separated from the acetone solution was washed 3 times with hot 2% alkali solution. The sodium carbonate and alkali solutions were combined, acidified with sulfuric acid, and extracted with ether. The ether was distilled off and the residue was crystallized from 60% acetic acid. 1.6 g of a white, finely crystalline material was obtained. After 2 recrystallizations from a mixture of methanol and water (2:1) the m.p. was 99-101°.

Found %: C 70.71; H 10.41; H (active) 0.81. Equiv. 257.1 $C_{15}H_{26}O_3$. Calculated %: C 70.86; H 10.23; H (active) 0.78. Equiv. = M 254.

The mother liquor after crystallization of the acid was a brown, thick liquid with a sharp odor.

The IR spectra and the Raman spectra were determined by us in the laboratories of the Leningrad State University and the Botanical Institute of the Academy of Sciences of the USSR under the direction of G. V. Pigulevskii.

SUMMARY

1. When sclareol was reacted with hydrogen chloride, the product obtained was a mixture of isomers of the composition $C_{20}H_{33}Cl$.   On the basis of the data from chemical and spectral analysis a structural formula has been proposed for one of the components.

2. When the monochloro derivative of sclareol was oxidized, an oxide $C_{20}H_{32}O$ and a hydroxy acid $C_{15}H_{26}O_3$ were isolated that had not been described in the literature.

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*Russian translation.

THE SAPOGENIN OF PATRINIA ROOTS

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In connection with an exploration of native flora undertaken by us for the purpose of developing plants containing steroidal compounds, we turned our attention to the plant Patrinia intermedia Roem. and Schult. (family valerianaceae); the roots of this plant were investigated by A. M. Sokol'skaya [1], who found in them a rather high saponin content, and ascribed a steroidal nature to the sapogenin obtained from it and proposed for it a structural formula with little basis. In view of the fact that some data presented in the publication cited elicited doubt, we investigated this plant anew.

As material for our investigation we used roots of Patrinia collected by an expedition from our Institute under the direction of P. S. Massagetov in July 1954 on the sands at Lake Issyk-Kul'; part of the experiments were carried out with Patrinia roots obtained from the Irzheval'sk ZOS VILAR. The two samples gave exactly the same results.

The saponin was obtained by treatment of the roots with methanol and precipitation from the methanol extract with ether; the yield agreed with that indicated by A. M. Sokol'skaya [1]. When the saponin was hydrolyzed by heating it with dilute sulfuric acid, a sapogenin was obtained that formed a difficultly soluble sodium salt; this indicated that the sapogenin was acid in nature. The free sapogenin isolated from the sodium salt had the composition $C_{30}H_{48}O_3$; its properties and those of its derivatives conformed with the properties of oleanolic acid and its derivatives. The infrared absorption spectra of the crystalline acetates of the sapogenin and oleanolic acid agreed completely.

The method used by us for processing the plant material was basically similar to that employed by A. M. Sokol'skaya [1], and the yield of sapogenin obtained by us, calculated on the amount of plant material, was close to that given in the article cited, in spite of the fact that we purified the sapogenin through the sodium salt. Therefore, we are inclined to think that the sapogenin obtained by A. M. Sokol'skaya was oleanolic acid. Such an assumption is also favored by the data from the elementary analysis of the sapogenin, which are given in in the publication cited [1] and which agree better with the formula $C_{30}H_{48}O_3$ than with the formula $C_{21}H_{32}O_2$ suggested by the above-mentioned author.

EXPERIMENTAL

Isolation of the saponin. 100 g of ground, air-dried Patrinia roots were extracted with 80% methanol in a Soxhlet apparatus for 16 hours; the extract was separated by filtration from a small amount of flocculent precipitate and the saponin was precipitated with three volumes of ether; the precipitate was filtered off, washed with ether, and dried at 80°; the yield of technical saponin was 13.3 g. It was a brownish powder, which did not give a compound with cholesterol.

Hydrolysis of the saponin and isolation of the sapogenin. 10 g of the saponin and 100 ml of 5% sulfuric acid were heated on a boiling water bath for 5 hours; separation of precipitate started in 40-50 minutes after the heating was begun. The precipitate was filtered out in a Buchner funnel, with cooling, carefully washed with water, dried at 100°, and dissolved in ether; the ether solution was shaken with 1 N sodium hydroxide solution, upon which a crystalline precipitate of the sodium salt of the sapogenin separated out in the aqueous layer; the liquid was removed by suction and the salt was washed with ether and 1 N sodium hydroxide solution,

dissolved in 70% methanol, the solution was boiled with carbon for 2 hours, filtered hot, and acidified with acetic acid; the crystalline sapogenin that precipitated on cooling was filtered off, washed with 70% methanol, and dried; yield 1.5 g. After recrystallization (several times) from hot methanol, needles were obtained with m.p. 306-308°, $[\alpha]_D^{20}$ + 83.6° (c 0.8). The sapogenin gave no depression in melting point when mixed with oleanolic acid (m.p. 307-308°) prepared by us from mistletoe leaves [2].

The acetate of the sapogenin was prepared by boiling the sapogenin with 10 parts of acetic anhydride for 30 minutes; after recrystallization from acetone the m.p. was 265-267°, $[\alpha]_D^{20}$ + 74.8° (c 0.7). The elementary composition corresponded to the formula $C_{32}H_{50}O_4$.

The methyl ester was prepared by the action of an ether solution of diazomethane on a suspension of the sapogenin in ether, whereupon the material went into solution rather rapidly with the evolution of nitrogen; after the ether was distilled off and the residue was recrystallized from acetone, the m.p. was 197-200°, $[\alpha]_D^{21}$ + 75.7° (c 1); literature data [3]: 197-198°, $[\alpha]_D$ + 75°. The elementary composition corresponded to the formula $C_{31}H_{50}O_3$.

The acetate of the methyl ester was prepared by the action of diazomethane on the acetate of the sapogenin. After recrystallization from alcohol, flakes were obtained with m.p. 220-221°, $[\alpha]_D^{20}$ + 66.5° (c 0.9); literature data [4]: m.p. 218-220°, $[\alpha]_D$ + 66.7°. The elementary composition corresponded to the formula $C_{33}H_{52}O_4$.

All three derivatives of the sapogenin gave no depression in melting point when mixed with the corresponding derivatives of oleanolic acid.

The specific rotation was determined in chloroform in all cases.

SUMMARY

A sapogenin obtained as the principal product from the hydrolysis of the saponin of the roots of the plant Patrinia intermedia Roem and Schult. was oleanolic acid.

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•As in original. — Publisher's note.
• •Original Russian pagination. See C.B. translation.

DISCUSSION

BROMINATION OF CYCLIC KETONES WITH THE AID OF DIOXAN DIBROMIDE

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I. V. Marchinskaya and A. S. Podberezina [1] recently published a paper entitled, "The problem of the bromination of cyclic ketones with the aid of dioxan dibromide. "Using the method of bromination proposed by L. A. Yanovskaya and A. P. Terent'ev [2,3], the authors did not succeed in preparing monobromocyclohexanone, from which fact they drew an erroneous conclusion regarding the uselessness of dioxan dibromide for the preparation of monobromoketones.

We consider it necessary to state that this method has been repeatedly checked by a number of authors (for example, [4]) and always has given well-defined results. In particular, the bromination of cyclohexanone with the aid of dioxan dibromide has been successfully carried out by students in the course of their practice in organic chemistry. The failure encountered by the authors is explained by a number of deviations from the procedure for carrying out the bromination as described by Yanovskaya, consisting first in the fact that the brominating agent and the ketone were not used in equimolecular quantities (0.3 mole of dioxan dibromide to 0.13 mole of cyclohexanone). In addition, the ketone was run into the dioxan dibromide solution, which also increased the relative amount of the latter. It is perfectly clear that under such circumstances it would be impossible to expect the formation of monobromocyclohexanone. Secondly, in the reaction process a rise in temperature was permitted (self-heating of the solution), which also promoted formation of the dibromoketone.

In preparing the monobromo-substituted ketones by the method of L. A. Yanovskaya, it is necessary to maintain the following conditions. 1) An equimolecular quantity of previously prepared dioxan dibromide is added in small portions, with cooling and stirring, to a solution of the ketone in ether or dioxan. During this process each portion is added only after complete decoloration of the preceding portion. It is sometimes necessary to wait 2-5 minutes for the reaction to start (decoloration of the first portion of dioxan dibromide). In a number of cases it is also useful to warm the solution slightly or to add to it 2-3 drops of concentrated hydrochloric acid. After the beginning of the reaction the decoloration of subsequent portions of dioxan dibromide is almost instantaneous. 2) In the bromination process, in most instances, it is necessary to cool the ketone solution with ice. 3) As a result of the slight stability of the α-bromoketones, it is necessary to carry out the removal of the solvent and the distillation of the bromo-derivative in a current of nitrogen in vacuo at the lowest pressure possible in order to reduce tar formation. The yields of monobromocyclohexanone by this method are 45-65%, depending on the skill of the experimenter.

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LETTERS TO THE EDITOR

NEW DERIVATIVES OF AZULENE

F. N. Stepanov and N. A. Aldanova

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Several groups of investigators [1] have recently described colored derivatives of azulene in which the nucleus of the latter is a part of the chromophoric system. The tropyl ring of azulene plays the role in these compounds of one electron donor-acceptor group (auxochrome), while either an oxygen atom or a nitrogen atom serves as the other auxochrome.

We * have prepared salts (I) that have the properties of typical basic dyes. The colored cation of the compound does not contain heteroatoms, and the seven-membered rings play in it the role of the two auxochromes. As far as we know, this is the first example of salt-type dyes whose colored cation is a hydrocarbon group.

(I)
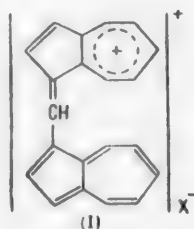
The perchlorate and chloride of the dye (I) $(X^- = ClO_4^-$ and Cl^- respectively) were obtained in quantitative yield by heating slightly, for a short time, a solution of azulene in orthoformic ester with a small excess of the appropriate acid. The dye that was formed precipitated slowly as an almost black, slightly bronzing powder. The chloride, moreover, was prepared by the condensation of azulene-2-aldehyde [2] with azulene in methyl alcohol solution in the presence of a small excess of hydrochloric acid. The latter reaction definitely confirms structure (I) for the dye obtained, the cation of which may be called diazulenyl-2-methene.

The perchlorate was rather difficultly soluble in the lower alcohols and chloroform, insoluble in water and ether. The chloride was considerably more soluble in alcohols and in water, too. The two salts did not melt when heated, but decomposed above 200°.

The absorption spectrum of the new dye was characterized in alcohol solution by a maximum at 617 m μ, 61700.

The deeply colored solutions of the dye were reversibly decolorized by alkalization. Ether extracted from the alkaline solution a light-yellow substance which gave the starting dye with acids. The new compound, which appeared to be a carbinol, has not yet been satisfactorily purified (m.p. 73-76°). When recrystallization was attempted, the material lost its solubility in ether and alcohols, going over, most probably, to a polymer.

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* 1. A report was presented at the meeting of the Academy of Sciences of the USSR entitled, "The problem of aromaticity and new carbocyclic aromatic systems" on April 8, 1958 in Moscow.

2. After the present communication was prepared for printing, No. 13 of the Z. Ang. Chem. was received in Moscow, in which (p. 413) there was reported the content of a paper by K. Hafner, who also had prepared a methine dye from azulene.

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SYNTHESIS OF O-PEPTIDES WITH THE AID OF
N,N'-DICYCLOHEXYLCARBODIIMIDE

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Institute of Biological and Medicinal Chemistry of the Academy of Medical
Sciences USSR.

The synthesis and study of the properties of O-peptides of β-hydroxy-α-amino acids is of great interest in connection with the ever-increasing biochemical significance of compounds of this type. However, in many instances their synthesis is associated with considerable difficulties. Now we have found a simple method for the preparation of O-peptides that consists in the condensation of esters of N-acylated hydroxyamino acids with N-acylamido acids by means of N,N'-dicyclohexylcarbodiimide. The reaction is carried out in the presence of pyridine, in acetone medium (or other organic solvents) at 20° for 24 hours. In this way, for example, we prepared the following compounds.

1) From the ethyl ester of N-benzoylserylglycine and carbobenzoxyleucine we obtained the ethyl ester of O-carbobenzoxyleucyl-N-benzoylserylglycine in 84% yield; m.p. 118° [from a mixture of ethyl acetate and petroleum ether (1:1)]. Found %: C 62.27; H 6.66; N 7.81; $C_{28}H_{35}O_{8}N_{3}$. Calculated %: C 62.09; H 6.51; N 7.76.

2) From the ethyl ester of N-benzoylserylglycine and carbobenzoxyphenylalanine we obtained the ethyl ester of O-carbobenzoxyphenylalanyl-N-benzoylserylglycine in 82% yield with m.p. 140° (from CCl$_4$). Found %: C 65.06; H 6.10; N 7.33. $C_{31}H_{33}O_{8}N_{3}$. Calculated %: C 64.68; H 5.78; N 7.30.

Furthermore, under similar conditions we obtained from the amide of salicylic acid and carbobenzoxyphenylalanine an 85% yield of the amide of O-carbobenzoxyphenylalanylsalicylic acid; m.p. 172° [1] (from alcohol).

LITERATURE CITED

[1] M. Brenner, J. P. Zimmermann, J. Wehrmuller, P. Quitt, A. Hartmann, W. Schneider and U. Beglinger, Helv. Chim. Acta, 40, 1497 (1957).

In conjunction with the State Committee on Chemistry of the Council of Ministers USSR and Moscow State University, the Division of Chemical Sciences Academy of Sciences USSR intends to hold the XI th All-Union Conferences on High-Molecular Compounds in Moscow in June 1959; the Conference will be devoted to the main problems of the processing and use of polymeric materials.

The following subjects for communications are proposed.

1. Anticorrosive material.

2. Dielectrics.

3. Rubber and synthetic rubber.

4. Chemical fibers.

5. Polymeric materials in building.

6. Methods of testing polymeric materials.

7. The processing of plastics.

8. Polymeric materials in machine construction.

9. Films, conservation, packing.

Persons and organizations wishing to participate in the Conference should present theses of up to 3 pages of typewritten text (in double spacing) before February 15, 1959 to the organizing committee of the XIth All-Union Conference on High-Molecular Compounds to the address: Moscow V-71, Lenin Avenue, d. 14, Division of Chemical Sciences Academy of Sciences USSR.

The communications should be limited to 10-15 minutes.

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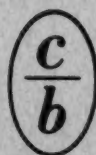
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